



Clinical trial results:

A RANDOMISED, DOUBLE-BLIND, PLACEBO CONTROLLED, MULTI-CENTER STUDY TO INVESTIGATE THE USE OF MEPOLIZUMAB (SB-240563) IN REDUCING THE NEED FOR SURGERY IN SUBJECTS WITH SEVERE BILATERAL NASAL POLYPOSIS

Summary

EudraCT number	2008-003772-21
Trial protocol	NL GB BE
Global end of trial date	05 December 2014

Results information

Result version number	v1
This version publication date	22 April 2016
First version publication date	16 August 2015

Trial information

Trial identification

Sponsor protocol code	MPP111782
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To define the effect of mepolizumab in reducing the need for surgery, defined as reduced endoscopic polyp score and symptom score after six months of dosing.
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Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 May 2009
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	United Kingdom: 38
Country: Number of subjects enrolled	Belgium: 36
Country: Number of subjects enrolled	Netherlands: 33
Worldwide total number of subjects	107
EEA total number of subjects	107

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)	95
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At the end of a 10- to 14-day Run-in Period, participants were assessed for entry into the Treatment Period, comprised of 8 outpatient visits. For 6 of these visits, participants received a dose of either 750 milligrams (mg) mepolizumab or placebo. Dosing occurred in 4-week intervals.

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	Mepolizumab 750 mg

Arm description:

Participants received a total of six doses (one every 4 weeks) of mepolizumab 750 milligrams (mg) by intravenous infusion.

Arm type	Experimental
Investigational medicinal product name	Mepolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

750 milligrams (mg) mepolizumab by intravenous (IV) infusion over 30 minutes

Arm title	Placebo
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Arm description:

Participants received a total of six doses (one every 4 weeks) of matching placebo by intravenous infusion.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo by IV infusion over 30 minutes

Number of subjects in period 1^[1]	Mepolizumab 750 mg	Placebo
Started	54	51
Completed	22	19
Not completed	32	32
Did Not Meet Continuation Criteria	17	11
Consent withdrawn by subject	2	1
Adverse event, non-fatal	3	5
Protocol-defined Stopping Criteria	-	1
Lost to follow-up	-	2
Lack of efficacy	5	11
Protocol deviation	5	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: Baseline data are reported for those enrolled participants comprising the Intent-to-Treat Population, defined as randomized participants who received at least one dose of study treatment.

Baseline characteristics

Reporting groups

Reporting group title	Mepolizumab 750 mg
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Reporting group description:

Participants received a total of six doses (one every 4 weeks) of mepolizumab 750 milligrams (mg) by intravenous infusion.

Reporting group title	Placebo
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Reporting group description:

Participants received a total of six doses (one every 4 weeks) of matching placebo by intravenous infusion.

Reporting group values	Mepolizumab 750 mg	Placebo	Total
Number of subjects	54	51	105
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	50.6	49.7	
standard deviation	± 10.73	± 10.38	-
Gender categorical			
Units: Subjects			
Female	13	17	30
Male	41	34	75
Race, Customized			
Units: Subjects			
Central/South Asian Heritage (Htg)	2	0	2
Japanese/East Asian Heritage/ South East Asian Htg	0	1	1
White	52	50	102

End points

End points reporting groups

Reporting group title	Mepolizumab 750 mg
Reporting group description:	
Participants received a total of six doses (one every 4 weeks) of mepolizumab 750 milligrams (mg) by intravenous infusion.	
Reporting group title	Placebo
Reporting group description:	
Participants received a total of six doses (one every 4 weeks) of matching placebo by intravenous infusion.	

Primary: Number of participants with a reduced need for surgery at the end of the study (Week 25)

End point title	Number of participants with a reduced need for surgery at the end of the study (Week 25)
End point description:	
Assessment of the nasal polyposis condition was performed after six months of dosing to determine the situation indicative of a reduction in the need for surgery. The components used to determine the need for surgery were endoscopic polyp scores and a severity of condition as measured by a visual analogue scale (VAS). Surgery was still deemed required for a participant with an ENP score of ≥ 3 , or an ENP score of 2 and a VAS symptom score of > 7 . The number of participants with reduced need for polyp surgery are presented as missing data set to non-responders (NR) and missing data last observation carry forward (LOCF). LOCF is defined as missing responses at Week 25 imputed with the last non-missing post-dose observation for that participant. The Per Protocol (PP) Population is comprised of all randomized participants who received at least one dose of study treatment and who complied with the protocol.	
End point type	Primary
End point timeframe:	
Week 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[1]	51 ^[2]		
Units: participants				
NR, Responders	16	5		
NR, Non-Responders	33	46		
LOCF, Responders	17	8		
LOCF, Non- Responders	32	43		

Notes:

[1] - PP Population

[2] - PP Population

Statistical analyses

Statistical analysis title	Statistical Analysis of NR
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Fisher exact

Statistical analysis title	Statistical Analysis of LOCF
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Fisher exact

Secondary: Number of participants with endoscopic nasal polyp (ENP) score dynamics at Screening and Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Number of participants with endoscopic nasal polyp (ENP) score dynamics at Screening and Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Each nostril was assessed for polyps and graded at Screening and at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. The ENP score ranges from 0 (no polyps) to 4, with a higher score indicating a larger polyp. The ENP score was recorded for both the right and the left nostril. The higher of the two scores was derived and used for the analysis. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Screening; Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[3]	51 ^[4]		
Units: participants				
Week 1, ENP score 0, n=49, 51	0	0		
Week 1, ENP score 1, n=49, 51	0	0		
Week 1, ENP score 2, n=49, 51	0	0		
Week 1, ENP score >=3, n=49, 51	49	51		
Week 2, ENP score 0, n=48, 51	0	0		
Week 2, ENP score 1, n=48, 51	0	0		
Week 2, ENP score 2, n=48, 51	1	0		
Week 2, ENP score >=3, n=48, 51	47	51		
Week 5, ENP score 0, n=49, 48	0	0		
Week 5, ENP score 1, n=49, 48	0	0		
Week 5, ENP score 2, n=49, 48	8	6		
Week 5, ENP score >=3, n=49, 48	41	42		

Week 9, ENP score 0, n=49, 45	0	0		
Week 9, ENP score 1, n=49, 45	5	0		
Week 9, ENP score 2, n=49, 45	8	5		
Week 9, ENP score >=3, n=49, 45	36	40		
Week 13, ENP score 0, n=44, 37	3	0		
Week 13, ENP score 1, n=44, 37	5	0		
Week 13, ENP score 2, n=44, 37	5	2		
Week 13, ENP score >=3, n=44, 37	31	35		
Week 17, ENP score 0, n=43, 34	3	1		
Week 17, ENP score 1, n=43, 34	4	1		
Week 17, ENP score 2, n=43, 34	7	6		
Week 17, ENP score >=3, n=43, 34	29	26		
Week 21, ENP score 0, n=42, 34	4	1		
Week 21, ENP score 1, n=42, 34	6	2		
Week 21, ENP score 2, n=42, 34	5	4		
Week 21, ENP score >=3, n=42, 34	27	27		
Week 25, ENP score 0, n=41, 31	3	1		
Week 25, ENP score 1, n=41, 31	7	2		
Week 25, ENP score 2, n=41, 31	7	4		
Week 25, ENP score >=3, n=41, 31	24	24		

Notes:

[3] - PP Population

[4] - PP Population

Statistical analyses

Statistical analysis title	Week 1
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[5]
P-value	= 0.708
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	3.63

Notes:

[5] - ordinal logistic model with random subject effects

Statistical analysis title	Week 2
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[6]
P-value	= 0.675
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	6.85

Notes:

[6] - ordinal logistic model with random subject effects

Statistical analysis title	Week 5
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[7]
P-value	= 0.943
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	4.49

Notes:

[7] - ordinal logistic model with random subject effects

Statistical analysis title	Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[8]
P-value	= 0.091
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	18.94

Notes:

[8] - ordinal logistic model with random subject effects

Statistical analysis title	Week 13
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Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[9]
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.18
upper limit	62.19

Notes:

[9] - ordinal logistic model with random subject effects

Statistical analysis title	Week 17
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[10]
P-value	= 0.223
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	13.9

Notes:

[10] - ordinal logistic model with random subject effects

Statistical analysis title	Week 21
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[11]
P-value	= 0.037
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	30.66

Notes:

[11] - ordinal logistic model with random subject effects

Statistical analysis title	Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[12]
P-value	= 0.047
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	28.42

Notes:

[12] - ordinal logistic model with random subject effects

Secondary: Number of participants who required polyp surgery at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Number of participants who required polyp surgery at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Assessment of the nasal polyposis condition was performed after 6 months of dosing to determine the situation indicative of a reduction in the need for surgery. The components used to determine the need for surgery were endoscopic polyp scores and a severity of condition as measured by a VAS. Surgery was required for participants with ENP scores of ≥ 3 , or ENP scores of 2 and a VAS symptom score of ≥ 7 .

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[13]	51 ^[14]		
Units: participants				
Week 1	49	51		
Week 2	48	51		
Week 5	44	49		
Week 9	39	48		
Week 13	38	50		
Week 17	37	46		
Week 21	35	46		
Week 25	33	46		

Notes:

[13] - PP Population

[14] - PP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Weeks 2, 5, 9, 13, 21, and 25

End point title	Mean change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Weeks 2, 5, 9, 13, 21, and 25
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End point description:

SBP and DBP were measured at Baseline (Week 1) and at Weeks 2, 5, 9, 13, 17, 21, and 25. Baseline is defined as the Week 1 pre-dose assessment. Change from Baseline is defined as the difference between the post-dose post-Baseline visit value and the Baseline value. The Safety Population is comprised of all participants who received at least one dose of study treatment. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[15]	51 ^[16]		
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Week 2, n=53, 52	-2 (± 14.14)	4.6 (± 13.33)		
SBP, Week 5, n=53, 49	-1.2 (± 11.74)	0.5 (± 10.5)		
SBP, Week 9, n=51, 46	-0.9 (± 15.01)	1 (± 12.84)		
SBP, Week 13, n=45, 40	-2.9 (± 12.17)	0.9 (± 11.97)		
SBP, Week 17, n=45, 36	-1.9 (± 13.15)	0.3 (± 11.72)		
SBP, Week 21, n=42, 34	-2 (± 14.55)	-1.7 (± 12.14)		
SBP, Week 25, n=42, 32	-2.4 (± 15.47)	-1.8 (± 15.39)		
DBP, Week 2, n=53, 52	-1.3 (± 7.97)	-0.9 (± 10.44)		
DBP, Week 5, n=53, 49	0 (± 8.56)	-0.1 (± 7.98)		
DBP, Week 9, n=51, 46	-1.8 (± 12.05)	0 (± 7.29)		
DBP, Week 13, n=45, 40	-0.6 (± 9.99)	-0.5 (± 9.56)		
DBP, Week 17, n=45, 36	-2.2 (± 8.9)	-0.4 (± 9.43)		
DBP, Week 21, n=42, 34	-0.3 (± 7.95)	-1.5 (± 9.32)		
DBP, Week 25, n=42, 32	-1.5 (± 10.27)	-2.2 (± 9.58)		

Notes:

[15] - Safety Population

[16] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in pulse rate at Weeks 2, 5, 9, 13, 17, 21, and 25

End point title	Mean change from Baseline in pulse rate at Weeks 2, 5, 9, 13, 17, 21, and 25
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End point description:

Pulse rate was measured at Baseline (Week 1) and at Weeks 2, 5, 9, 13, 17, 21, and 25. Baseline is

defined as the Week 1 pre-dose assessment. Change from Baseline is defined as the difference between the post-dose post-Baseline visit value and the Baseline value. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 2, 5, 9, 13, 17, 21, and 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[17]	51 ^[18]		
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 2, n=53, 52	0.2 (± 8.88)	0 (± 7.86)		
Week 5, n=53, 50	-1.1 (± 9.09)	-1 (± 7.91)		
Week 9, n=51, 46	-1.7 (± 8.4)	-0.8 (± 7.5)		
Week 13, n=45, 40	-0.4 (± 11.05)	-2.4 (± 9.42)		
Week 17, n=45, 36	-0.4 (± 9.71)	-0.6 (± 9.35)		
Week 21, n=41, 34	-2 (± 9.56)	-1.2 (± 8.7)		
Week 25, n=41, 32	-0.4 (± 9.29)	0 (± 8.29)		

Notes:

[17] - Safety Population

[18] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated electrocardiogram (ECG) findings at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Number of participants with the indicated electrocardiogram (ECG) findings at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

A single safety 12-lead ECG was performed using a standard 12-lead ECG machine at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Any abnormal clinically significant (CS) and not clinically significant (NCS) findings were identified. ECG abnormality with respect to CS and NCS findings were judged by the investigator or appropriately qualified designee. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
End point timeframe:	
Weeks 1, 2, 5, 9, 13, 17, 21, and 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[19]	51 ^[20]		
Units: participants				
Week 1, NCS, n=53, 52	8	8		
Week 1, CS, n=53, 52	0	0		
Week 2, NCS, n=52, 52	7	9		
Week 2, CS, n=52, 52	0	0		
Week 5, NCS, n=53, 50	8	8		
Week 5, CS, n=53, 50	0	0		
Week 9, NCS, n=52, 46	5	3		
Week 9, CS, n=52, 46	0	0		
Week 13, NCS, n=45, 40	6	4		
Week 13, CS, n=45, 40	0	0		
Week 17, NCS, n=45, 36	9	4		
Week 17, CS, n=45, 36	0	0		
Week 21, NCS, n=42, 34	3	1		
Week 21, CS, n=42, 34	0	0		
Week 25, NCS, n=41, 31	2	3		
Week 25, CS, n=41, 31	0	0		

Notes:

[19] - Safety Population

[20] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of clinical chemistry parameters including blood urea nitrogen (BUN), glucose fasting, chloride, sodium, potassium, carbon dioxide, and calcium at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of clinical chemistry parameters including blood urea nitrogen (BUN), glucose fasting, chloride, sodium, potassium, carbon dioxide, and calcium at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

BUN, glucose fasting, chloride, sodium, potassium, carbon dioxide (CO₂), and calcium were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[21]	51 ^[22]		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				

Calcium, Week 1, pre-dose, n=46, 46	2.33529 (\pm 0.0792)	2.31724 (\pm 0.08132)		
Calcium, Week 2, n=53, 52	2.34262 (\pm 0.07908)	2.35237 (\pm 0.09561)		
Calcium, Week 5, pre-dose, n=52, 49	2.31874 (\pm 0.09841)	2.34182 (\pm 0.09948)		
Calcium, Week 9, pre-dose, n=52, 46	2.31885 (\pm 0.07624)	2.36803 (\pm 0.18232)		
Calcium, Week 13, pre-dose, n=44, 40	2.32566 (\pm 0.07731)	2.34848 (\pm 0.08552)		
Calcium, Week 17, pre-dose, n=45, 35	2.31207 (\pm 0.09495)	2.3561 (\pm 0.10049)		
Calcium, Week 21, pre-dose, n=42, 34	2.30473 (\pm 0.08874)	2.32699 (\pm 0.10993)		
Calcium, Week 25, 4 weeks post last dose, n=41, 32	2.31374 (\pm 0.13942)	2.36884 (\pm 0.08507)		
Chloride, Week 1, pre-dose, n=50, 51	103.7 (\pm 2.57)	103.8 (\pm 2.52)		
Chloride, Week 2, n=50, 51	103.8 (\pm 2.23)	103.5 (\pm 2.39)		
Chloride, Week 5, pre-dose, n=51, 49	103.5 (\pm 3.24)	103.6 (\pm 2.34)		
Chloride, Week 9, pre-dose, n=51, 44	103.7 (\pm 2.85)	103.6 (\pm 2.33)		
Chloride, Week 13, pre-dose, n=45, 40	103.4 (\pm 2.36)	103.2 (\pm 2.55)		
Chloride, Week 17, pre-dose, n=45, 34	103.6 (\pm 2.72)	103.4 (\pm 2.32)		
Chloride, Week 21, pre-dose, n=42, 34	103.6 (\pm 2.55)	103.4 (\pm 2.53)		
Chloride, Week 25, 4 weeks post last dose, n=40,32	103 (\pm 2.36)	103.2 (\pm 2.73)		
CO2, Week 1, pre-dose, n=47, 51	27.3 (\pm 2.38)	26.4 (\pm 2.31)		
CO2, Week 2, n=50, 50	26.5 (\pm 2.71)	26.4 (\pm 2.36)		
CO2, Week 5, pre-dose, n=50, 50	26.4 (\pm 2.76)	26.1 (\pm 2.66)		
CO2, Week 9, pre-dose, n=51, 45	27.2 (\pm 2.63)	26.1 (\pm 2.81)		
CO2, Week 13, pre-dose, n=45, 38	27.4 (\pm 2.32)	26.4 (\pm 2.11)		
CO2, Week 17, pre-dose, n=45, 34	26.4 (\pm 2.98)	26.3 (\pm 2.31)		
CO2, Week 21, pre-dose, n=40, 34	27.2 (\pm 2.05)	26.4 (\pm 2.39)		
CO2, Week 25, 4 weeks post last dose, n=41, 32	27.2 (\pm 2.73)	27 (\pm 2.21)		
Glucose, Week 1, pre-dose, n=49, 51	5.02333 (\pm 1.06419)	4.90943 (\pm 0.55713)		
Glucose, Week 2, n=49, 45	5.07525 (\pm 0.94855)	4.85985 (\pm 0.69818)		
Glucose, Week 5, pre-dose, n=52, 49	4.97329 (\pm 0.75574)	4.97545 (\pm 0.68857)		
Glucose, Week 9, pre-dose, n=50, 44	5.07978 (\pm 0.82661)	5.01449 (\pm 0.70049)		
Glucose, Week 13, pre-dose, n=45, 40	5.09957 (\pm 0.90555)	4.95848 (\pm 0.63337)		
Glucose, Week 17, pre-dose, n=44, 34	5.19291 (\pm 1.20604)	4.99349 (\pm 0.65387)		
Glucose, Week 21, pre-dose, n=40, 33	5.12557 (\pm 1.14974)	5.01559 (\pm 0.55765)		
Glucose, Week 25, 4 weeks post last dose, n=40, 31	5.31222 (\pm 1.55173)	5.08589 (\pm 0.57875)		
Potassium, Week 1, pre-dose, n=52, 52	4.11 (\pm 0.352)	4.17 (\pm 0.353)		
Potassium, Week 2, n=53, 51	4.26 (\pm 0.345)	4.23 (\pm 0.312)		
Potassium, Week 5, pre-dose, n=51, 49	4.1 (\pm 0.42)	4.15 (\pm 0.357)		
Potassium, Week 9, pre-dose, n=52, 45	4.13 (\pm 0.364)	4.19 (\pm 0.432)		
Potassium, Week 13, pre-dose, n=45, 40	4.09 (\pm 0.325)	4.19 (\pm 0.378)		
Potassium, Week 17, pre-dose, n=44, 35	4.15 (\pm 0.389)	4.28 (\pm 0.438)		

Potassium, Week 21, pre-dose, n=40, 34	4.19 (± 0.428)	4.27 (± 0.415)		
Potassium, Week 25, 4 weeks post last dose, n=41, 32	4.19 (± 0.404)	4.29 (± 0.376)		
Sodium, Week 1, pre-dose, n=52, 52	141.9 (± 2.15)	141.7 (± 2.15)		
Sodium, Week 2, n=53, 51	142.1 (± 1.95)	141.5 (± 2.25)		
Sodium, Week 5, pre-dose, n=52, 49	141.7 (± 2.16)	141.7 (± 1.91)		
Sodium, Week 9, pre-dose, n=52, 46	142 (± 2.27)	141.5 (± 2.3)		
Sodium, Week 13, pre-dose, n=45, 40	141.8 (± 1.93)	141.4 (± 2.47)		
Sodium, Week 17, pre-dose, n=45, 35	141.6 (± 2.34)	141.5 (± 2.15)		
Sodium, Week 21, pre-dose, n=42, 34	141.5 (± 2.04)	141.6 (± 2.48)		
Sodium, Week 25, 4 weeks post last dose, n=41, 32	141.4 (± 2.11)	141.7 (± 2.36)		
Urea, Week 1, pre-dose, n=51, 51	7.6929 (± 3.6977)	7.1568 (± 3.35084)		
Urea, Week 2, n=52, 52	7.8847 (± 3.86054)	7.187 (± 3.81593)		
Urea, Week 5, pre-dose, n=52, 49	7.9122 (± 3.86267)	7.2488 (± 4.02159)		
Urea, Week 9, pre-dose, n=51, 46	7.5806 (± 3.77958)	7.0658 (± 3.40683)		
Urea, Week 13, pre-dose, n=45, 40	7.4124 (± 3.50688)	7.5311 (± 3.68104)		
Urea, Week 17, pre-dose, n=45, 35	7.3499 (± 3.6194)	7.9377 (± 3.595)		
Urea, Week 21, pre-dose, n=42, 34	7.7361 (± 3.58351)	7.2357 (± 3.21507)		
Urea, Week 25, 4 weeks post last dose, n=41, 32	7.877 (± 3.86299)	6.9864 (± 3.01889)		

Notes:

[21] - Safety Population

[22] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the clinical chemistry parameters of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma glutamyltransferase (GGT) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the clinical chemistry parameters of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma glutamyltransferase (GGT) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

ALT, AST, ALP, and GGT were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed. "99999" indicates that data are not available because either (1) no participants were analyzed for a parameter at a particular time point, or that (2) a standard deviation cannot be calculated because only one participant was analyzed for a parameter at a particular time point.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[23]	51 ^[24]		
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
ALP, Week 1, pre-dose, n=52, 52	76 (± 17.09)	67.8 (± 20)		
ALP, Week 2, n=53, 52	75.3 (± 15.92)	69 (± 20.91)		
ALP, Week 5, pre-dose, n=51, 50	75.1 (± 17.31)	68.5 (± 21.84)		
ALP, Week 9, pre-dose, n=51, 45	75.9 (± 17.63)	69.8 (± 20.88)		
ALP, Week 13, pre-dose, n=45, 40	75.1 (± 16.92)	69.7 (± 21.27)		
ALP, Week 17, pre-dose, n=45, 35	72.5 (± 16.3)	69.5 (± 19.58)		
ALP, Week 21, pre-dose, n=41, 34	72.4 (± 14.75)	70.4 (± 21.81)		
ALP, Week 25, 4 weeks post last dose, n=41, 32	73.9 (± 14.56)	72.4 (± 22.05)		
ALT, Week 1, pre-dose, n=52, 52	27.5 (± 13.33)	26.1 (± 14.85)		
ALT, Week 2, n=53, 51	26.3 (± 11.6)	26.9 (± 15.89)		
ALT, Week 5, pre-dose, n=51, 50	26.5 (± 15.11)	25 (± 13.36)		
ALT, Week 9, pre-dose, n=52, 45	26.4 (± 10.78)	24.7 (± 12.41)		
ALT, Week 13, pre-dose, n=45, 40	29.1 (± 18.21)	25.2 (± 11.18)		
ALT, Week 17, pre-dose, n=45, 35	25.7 (± 11.98)	27.1 (± 15.11)		
ALT, Week 21, pre-dose, n=42, 34	26.2 (± 14.32)	27.6 (± 14.02)		
ALT, Week 25, 4 weeks post last dose, n=41, 32	28.4 (± 15.43)	26.4 (± 13.18)		
AST, Week 1, pre-dose, n=52, 52	24.6 (± 7.73)	25.5 (± 9.13)		
AST, Week 2, n=51, 51	24.2 (± 5.54)	24.3 (± 7.51)		
AST, Week 5, pre-dose, n=51, 50	24.3 (± 6.51)	23.6 (± 6.61)		
AST, Week 9, pre-dose, n=51, 45	24.6 (± 6.06)	23.6 (± 5.94)		
AST, Week 13, pre-dose, n=45, 40	25.4 (± 6.86)	23.9 (± 6.04)		
AST, Week 17, pre-dose, n=44, 34	24 (± 8.34)	23.9 (± 6.42)		
AST, Week 21, pre-dose, n=40, 34	24.5 (± 6.2)	23.8 (± 5.18)		
AST, Week 25, 4 weeks post last dose, n=41, 32	25.1 (± 5.63)	24 (± 7.77)		
GGT, Week 1, pre-dose, n=50, 51	34.4 (± 49.18)	26.6 (± 20.37)		
GGT, Week 2, n=53, 52	32.6 (± 4.31)	28.3 (± 24.67)		
GGT, Week 5, pre-dose, n=50, 50	33.9 (± 59.91)	28 (± 25.08)		
GGT, Week 9, pre-dose, n=50, 44	33.7 (± 41.07)	29.5 (± 24.86)		
GGT, Week 13, pre-dose, n=45, 40	37.2 (± 69.6)	29.2 (± 21.56)		
GGT, Week 17, pre-dose, n=44, 34	34.8 (± 57.83)	34.6 (± 32.72)		
GGT, Week 21, pre-dose, n=41, 34	38.6 (± 78.78)	32.9 (± 27.27)		
GGT, Week 25, 4 weeks post last dose, n=41, 32	37 (± 54.09)	28.4 (± 17.24)		

Notes:

[23] - Safety Population

[24] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the clinical chemistry parameters of albumin and protein at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the clinical chemistry parameters of albumin
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End point description:

Albumin and protein were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type

Secondary

End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[25]	51 ^[26]		
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Albumin, Week 1, pre-dose, n=52, 52	46 (± 3)	46.1 (± 2.4)		
Albumin, Week 2, n=53, 52	45.2 (± 2.74)	46.3 (± 3.17)		
Albumin, Week 5, pre-dose, n=52, 50	45.2 (± 2.46)	45.8 (± 2.4)		
Albumin, Week 9, pre-dose, n=52, 46	45.3 (± 2.71)	45.2 (± 2.51)		
Albumin, Week 13, pre-dose, n=45, 40	45.1 (± 2.26)	45.8 (± 2.97)		
Albumin, Week 17, pre-dose, n=44, 35	44.8 (± 2.45)	45.6 (± 2.13)		
Albumin, Week 21, pre-dose, n=42, 34	45 (± 2.69)	45.1 (± 2.81)		
Albumin, Week 25, 4 weeks post last dose, n=41, 32	45.7 (± 2.55)	45.3 (± 2.5)		
Protein, Week 1, pre-dose, n=50, 48	73.1 (± 5.09)	73.7 (± 4.54)		
Protein, Week 2, n=52, 49	72.4 (± 5.27)	73.7 (± 5.3)		
Protein, Week 5, pre-dose, n=50, 49	72.8 (± 5.33)	72.6 (± 4.75)		
Protein, Week 9, pre-dose, n=51, 46	73 (± 5.39)	72.6 (± 4.5)		
Protein, Week 13, pre-dose, n=44, 40	73.1 (± 4.76)	72.8 (± 5.11)		
Protein, Week 17, pre-dose, n=45, 35	71.3 (± 4.08)	72.1 (± 4.26)		
Protein, Week 21, pre-dose, n=42, 34	71.3 (± 4.3)	71.4 (± 3.88)		
Protein, Week 25, 4 weeks post last dose, n=41, 32	72.1 (± 4.41)	71.7 (± 4.53)		

Notes:

[25] - Safety Population

[26] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the clinical chemistry parameters of total and direct bilirubin, creatinine (CRT), and uric acid (UA) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title

Absolute values of the clinical chemistry parameters of total and direct bilirubin, creatinine (CRT), and uric acid (UA) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point description:

Total and direct bilirubin, creatinine, and uric acid were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed. "99999" indicates that data are not available because either (1) no participants were analyzed for a parameter at a particular time point, or that (2) a standard deviation cannot be calculated because only one participant was analyzed for a parameter at a particular time point.

End point type

Secondary

End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[27]	51 ^[28]		
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
UA, Week 1, pre-dose, n=48, 50	6280.75 (± 40503.47)	9943.59 (± 47675.43)		
UA, Week 2, n=49, 49	7734.39 (± 50942.24)	10906.56 (± 51211.16)		
UA, Week 5, pre-dose, n=50, 49	12991.02 (± 65048.95)	13352.52 (± 64149.31)		
UA, Week 9, pre-dose, n=49, 44	13147.62 (± 62976.19)	24031.3 (± 90312.49)		
UA, Week 13, pre-dose, n=45, 40	14802.92 (± 69028.68)	25208.07 (± 90067.04)		
UA, Week 17, pre-dose, n=45, 35	15378.37 (± 70783.69)	21723.77 (± 89724.11)		
UA, Week 21, pre-dose, n=40, 34	10414.21 (± 63827.1)	22994.49 (± 94463.05)		
UA, Week 25, 4 weeks post last dose, n=40, 32	9602.1 (± 58607.26)	24506.63 (± 96050.66)		
CRT, Week 1, pre-dose, n=52, 52	80.2445 (± 15.7113)	77.5162 (± 14.87768)		
CRT, Week 2, n=53, 51	80.545 (± 14.66619)	78.362 (± 13.55791)		
CRT, Week 5, pre-dose, n=52, 49	79.0978 (± 14.80378)	77.7282 (± 13.97357)		
CRT, Week 9, pre-dose, n=52, 46	81.0171 (± 15.27077)	75.9868 (± 13.78284)		
CRT, Week 13, pre-dose, n=45, 40	81.5454 (± 17.47683)	77.5522 (± 13.18623)		
CRT, Week 17, pre-dose, n=45, 35	81.5074 (± 17.96973)	76.7809 (± 12.15771)		
CRT, Week 21, pre-dose, n=42, 34	80.8093 (± 17.58041)	75.1511 (± 11.77313)		
CRT, Week 25, 4 weeks post last dose, n=41, 32	81.9687 (± 17.48642)	77.7839 (± 12.25219)		
TB, Week 1, pre-dose, n=52, 52	9.878 (± 3.2705)	10.595 (± 6.2074)		
TB, Week 2, n=53, 52	10.016 (± 4.5747)	10.52 (± 4.1684)		
TB, Week 5, pre-dose, n=51, 50	10.189 (± 4.0635)	10.878 (± 4.4865)		
TB, Week 9, pre-dose, n=51, 45	10.145 (± 3.5212)	10.484 (± 4.2254)		
TB, Week 13, pre-dose, n=45, 40	9.918 (± 3.6143)	10.012 (± 5.0501)		
TB, Week 17, pre-dose, n=44, 35	10.624 (± 4.0522)	9.877 (± 4.6822)		
TB, Week 17, 4-6 months, n=2, 2	7 (± 2.8284)	7.775 (± 1.096)		
TB, Week 21, pre-dose, n=40, 34	10.266 (± 3.6078)	10.622 (± 6.0172)		

TB, Week 25, 4 weeks post last dose, n=41, 32	9.82 (± 3.0792)	10.162 (± 6.3294)		
DB, Week 1, pre-dose, n=50, 50	2.6685 (± 0.91566)	2.8818 (± 1.54541)		
DB, Week 2, n=53, 51	2.916 (± 1.0256)	3.069 (± 1.25759)		
DB, Week 5, pre-dose, n=49, 49	2.7981 (± 0.90148)	2.9939 (± 1.12944)		
DB, Week 9, pre-dose, n=51, 43	2.9203 (± 1.10282)	2.9693 (± 1.03703)		
DB, Week 13, pre-dose, n=43, 40	2.7958 (± 0.82254)	3.0299 (± 1.55388)		
DB, Week 17, pre-dose, n=43, 35	2.9931 (± 0.85581)	2.8714 (± 1.18421)		
DB, Week 17, 4-6 months, n=2, 2	1.9995 (± 0.00071)	2.197 (± 0.2786)		
DB, Week 21, pre-dose, n=39, 34	2.9267 (± 0.98861)	3.0561 (± 1.33234)		
DB, Week 25, 4 weeks post last dose, n=41, 32	3.0011 (± 0.95645)	2.9864 (± 1.42919)		

Notes:

[27] - Safety Population

[28] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the hematology parameters of platelet count and white blood cell (WBC) count, basophils, eosinophils, lymphocytes, monocytes, and neutrophils at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the hematology parameters of platelet count and white blood cell (WBC) count, basophils, eosinophils, lymphocytes, monocytes, and neutrophils at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Platelet count, WBC count, basophils, eosinophils, lymphocytes, monocytes, and neutrophils were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[29]	51 ^[30]		
Units: 10 ⁹ cells per liter				
arithmetic mean (standard deviation)				
Platelets, Week 1, pre-dose, n=52, 52	246.1 (± 45.91)	262.9 (± 53.61)		
Platelets, Week 2, n=53, 52	250.1 (± 47.25)	264.6 (± 56.54)		
Platelets, Week 5, pre-dose, n=53, 50	240.7 (± 46.67)	266.4 (± 61.2)		

Platelets, Week 9, pre-dose, n=51, 46	239.1 (± 43.29)	267 (± 57.64)		
Platelets, Week 13, pre-dose, n=45, 40	242.7 (± 53.68)	273.2 (± 56.18)		
Platelets, Week 17, pre-dose, n=45, 35	236.4 (± 45.59)	270.2 (± 52.58)		
Platelets, Week 21, pre-dose, n=42, 34	233 (± 44.39)	271.2 (± 53.89)		
Platelet, Week 25, 4 weeks post last dose, n=41,32	242.1 (± 48.64)	279.3 (± 60.44)		
WBC, Week 1, pre-dose, n=52, 52	7.16 (± 1.794)	6.81 (± 1.634)		
WBC, Week 2, n=53, 52	6.2 (± 1.535)	6.9 (± 2.014)		
WBC, Week 5, pre-dose, n=53, 50	6.17 (± 1.58)	6.77 (± 1.574)		
WBC, Week 9, pre-dose, n=51, 46	5.9 (± 1.508)	6.92 (± 1.553)		
WBC, Week 13, pre-dose, n=45, 40	5.93 (± 1.541)	7.18 (± 2.095)		
WBC, Week 17, pre-dose, n=45, 35	6.03 (± 1.78)	6.99 (± 1.916)		
WBC, Week 21, pre-dose, n=42, 34	5.86 (± 1.143)	6.92 (± 1.576)		
WBC, Week 25, 4 weeks post last dose, n=41, 32	5.93 (± 1.357)	7 (± 1.922)		
Basophils, Week 1, pre-dose, n=52, 52	0.05 (± 0.029)	0.05 (± 0.026)		
Basophils, Week 2, n=53, 51	0.03 (± 0.021)	0.05 (± 0.026)		
Basophils, Week 5, pre-dose, n=53, 50	0.02 (± 0.013)	0.05 (± 0.032)		
Basophils, Week 9, pre-dose, n=51, 45	0.03 (± 0.017)	0.05 (± 0.028)		
Basophils, Week 13, pre-dose, n=45, 40	0.03 (± 0.024)	0.06 (± 0.082)		
Basophils, Week 17, pre-dose, n=45, 35	0.03 (± 0.021)	0.05 (± 0.027)		
Basophils, Week 21, pre-dose, n=42, 34	0.03 (± 0.021)	0.05 (± 0.041)		
Basophils, Week 25, 4 weeks post last dose, n=41,32	0.03 (± 0.021)	0.05 (± 0.023)		
Eosinophils, Week 1, pre-dose, n=52, 52	0.063 (± 0.496)	0.54 (± 0.305)		
Eosinophils, Week 2, n=53, 52	0.1 (± 0.079)	0.55 (± 0.346)		
Eosinophils, Week 5, pre-dose, n=53, 50	0.05 (± 0.03)	0.051 (± 0.276)		
Eosinophils, Week 9, pre-dose, n=51, 46	0.04 (± 0.027)	0.55 (± 0.392)		
Eosinophils, Week 13, pre-dose, n=45, 40	0.07 (± 0.196)	0.056 (± 0.476)		
Eosinophils, Week 17, pre-dose, n=45, 35	0.05 (± 0.125)	0.45 (± 0.314)		
Eosinophils, Week 21, pre-dose, n=42, 34	0.04 (± 0.023)	0.49 (± 0.411)		
Eosinophil, Week 25, 4 weeks post last dose, n=41,32	0.04 (± 0.029)	0.44 (± 0.256)		
Lymphocytes, Week 1, pre-dose, n=52, 52	1.94 (± 0.568)	1.99 (± 0.615)		
Lymphocytes, Week 2, n=53, 52	1.84 (± 0.531)	1.96 (± 0.516)		
Lymphocytes, Week 5, pre-dose, n=53, 50	1.83 (± 0.635)	1.9 (± 0.466)		
Lymphocytes, Week 9, pre-dose, n=51, 46	1.83 (± 0.596)	2.03 (± 0.616)		
Lymphocytes, Week 13, pre-dose, n=45, 40	1.8 (± 0.457)	2.02 (± 0.555)		
Lymphocytes, Week 17, pre-dose, n=45, 35	1.77 (± 0.466)	1.92 (± 0.453)		
Lymphocytes, Week 21, pre-dose, n=42, 34	1.83 (± 0.541)	1.98 (± 0.514)		
Lymphocyte, Week 25, 4 weeks post last dose, n=41, 3	1.88 (± 0.604)	1.91 (± 0.523)		
Monocytes, Week 1, pre-dose, n=52, 51	0.56 (± 0.166)	0.5 (± 0.131)		

Monocytes, Week 2, n=53, 52	0.56 (± 1.75)	0.54 (± 0.19)		
Monocytes, Week 5, pre-dose, n=53, 50	0.53 (± 0.17)	0.51 (± 0.138)		
Monocytes, Week 9, pre-dose, n=51, 46	0.5 (± 0.14)	0.53 (± 0.163)		
Monocytes, Week 13, pre-dose, n=45, 40	0.5 (± 0.188)	0.55 (± 0.159)		
Monocytes, Week 17, pre-dose, n=45, 35	0.51 (± 0.172)	0.52 (± 0.142)		
Monocytes, Week 21, pre-dose, n=42, 34	0.5 (± 0.15)	0.55 (± 0.158)		
Monocytes, Week 25, 4 weeks post last dose, n=41, 32	0.51 (± 0.13)	0.57 (± 0.201)		
Neutrophils, Week 1, pre-dose, n=52, 52	3.96481 (± 1.374461)	3.72673 (± 1.085727)		
Neutrophils, Week 2, n=53, 52	3.65642 (± 1.295348)	3.80635 (± 1.525888)		
Neutrophils, Week 5, pre-dose, n=53, 50	3.73509 (± 1.238233)	3.7872 (± 1.237163)		
Neutrophils, Week 9, pre-dose, n=51, 45	3.49333 (± 1.160355)	3.76333 (± 1.095441)		
Neutrophils, Week 13, pre-dose, n=45, 39	3.524 (± 1.287322)	3.96169 (± 1.563461)		
Neutrophils, Week 17, pre-dose, n=45, 35	3.65711 (± 1.624295)	4.06657 (± 1.550068)		
Neutrophils, Week 21, pre-dose, n=42, 34	3.45738 (± 0.907831)	3.83824 (± 1.137039)		
Neutrophil, Week 25, 4 weeks post last dose, n=41, 3	3.46854 (± 1.045869)	4.03125 (± 1.452175)		

Notes:

[29] - Safety Population

[30] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the hematology parameters of hemoglobin and mean corpuscular hemoglobin concentration (MCHC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the hematology parameters of hemoglobin and mean corpuscular hemoglobin concentration (MCHC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
End point description:	Hemoglobin and MCHC were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.
End point type	Secondary
End point timeframe:	Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[31]	51 ^[32]		
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Hemoglobin, Week 1, pre-dose, n=51, 52	148.445 (± 11.5174)	145.566 (± 22.1192)		
Hemoglobin, Week 2, n=53, 52	148.013 (± 12.2563)	147.625 (± 11.1436)		
Hemoglobin, Week 5, pre-dose, n=53, 50	147.955 (± 10.886)	146.071 (± 12.7175)		
Hemoglobin, Week 9, pre-dose, n=51, 46	147.135 (± 11.0248)	146.252 (± 12.0539)		
Hemoglobin, Week 13, pre-dose, n=45, 40	147.498 (± 10.951)	147.427 (± 11.9305)		
Hemoglobin, Week 17, pre-dose, n=45, 35	145.988 (± 11.4327)	148.045 (± 12.0595)		
Hemoglobin, Week 21, pre-dose, n=42, 34	146.597 (± 11.8831)	146.953 (± 10.9213)		
Hemoglobin, Week 25, 4 weeks post last dose, n=41, 3	148.927 (± 10.5835)	147.94 (± 8.989)		
MCHC, Week 1, pre-dose, n=52, 51	338.3 (± 8.71)	338.6 (± 16.71)		
MCHC, Week 2, n=52, 52	338.1 (± 10.34)	335.2 (± 9.33)		
MCHC, Week 5, pre-dose, n=53, 50	338.1 (± 7.71)	338.6 (± 15.85)		
MCHC, Week 9, pre-dose, n=51, 46	336.5 (± 10.4)	337.7 (± 9.52)		
MCHC, Week 13, pre-dose, n=44, 40	338.7 (± 9.52)	339.6 (± 17.77)		
MCHC, Week 17, pre-dose, n=45, 35	338.6 (± 9.56)	337 (± 10.02)		
MCHC, Week 21, pre-dose, n=42, 34	338.9 (± 9.35)	336.4 (± 9.84)		
MCHC, Week 25, 4 weeks post last dose, n=40, 32	338.9 (± 9.23)	339.3 (± 18.86)		

Notes:

[31] - Safety Population

[32] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the hematology parameter of red blood cell (RBC) count and reticulocyte count (RC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the hematology parameter of red blood cell (RBC) count and reticulocyte count (RC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

RBC count and RC were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[33]	51 ^[34]		
Units: 10 ¹² cells per liter				
arithmetic mean (standard deviation)				
RBC, Week 1, pre-dose, n=52, 52	4.889 (± 0.3758)	4.93 (± 0.483)		
RBC, Week 2, n=53, 52	4.868 (± 0.4024)	4.937 (± 0.434)		
RBC, Week 5, pre-dose, n=53, 50	4.876 (± 0.3494)	4.867 (± 0.5115)		
RBC, Week 9, pre-dose, n=51, 46	4.875 (± 0.3792)	4.879 (± 0.4758)		
RBC, Week 13, pre-dose, n=45, 40	4.889 (± 0.3511)	4.923 (± 0.4828)		
RBC, Week 17, pre-dose, n=45, 35	4.824 (± 0.3735)	4.938 (± 0.5058)		
RBC, Week 21, pre-dose, n=42, 34	4.84 (± 0.3743)	4.91 (± 0.5165)		
RBC, Week 25, 4 weeks post last dose, n=41, 32	4.902 (± 0.3551)	4.901 (± 0.3343)		
RC, Week 1, pre-dose, n=28, 32	0.0537 (± 0.01651)	0.0495 (± 0.01666)		
RC, Week 2, n=33, 35	0.0495 (± 0.01682)	0.0506 (± 0.01879)		
RC, Week 5, pre-dose, n=33, 33	0.0461 (± 0.01416)	0.0496 (± 0.0253)		
RC, Week 9, pre-dose, n=29, 29	0.0443 (± 0.01327)	0.0513 (± 0.02581)		
RC, Week 13, pre-dose, n=28, 23	0.0473 (± 0.0153)	0.0528 (± 0.0178)		
RC, Week 17, pre-dose, n=28, 20	0.0482 (± 0.01604)	0.0493 (± 0.01847)		
RC, Week 21, pre-dose, n=26, 19	0.0459 (± 0.01592)	0.0521 (± 0.01594)		
RC, Week 25, 4 weeks post last dose, n=24, 20	0.0489 (± 0.0164)	0.058 (± 0.02625)		

Notes:

[33] - Safety Population

[34] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the hematology parameter of mean corpuscular hemoglobin (MCH) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the hematology parameter of mean corpuscular hemoglobin (MCH) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

MCH was assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
End point timeframe:	
Weeks 1, 2, 5, 9, 13, 17, 21, and 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[35]	51 ^[36]		
Units: Picograms (pg)				
arithmetic mean (standard deviation)				
Week 1, pre-dose, n=52, 51	30.44 (± 1.215)	30.26 (± 1.804)		
Week 2, n=52, 52	30.46 (± 1.359)	29.94 (± 1.631)		
Week 5, pre-dose, n=53, 50	30.37 (± 1.301)	30.1 (± 1.686)		
Week 9, pre-dose, n=51, 46	30.23 (± 1.378)	30.07 (± 1.793)		
Week 13, pre-dose, n=44, 40	30.22 (± 1.292)	29.94 (± 2.187)		
Week 17, pre-dose, n=45, 35	30.29 (± 1.339)	30.1 (± 1.951)		
Week 21, pre-dose, n=42, 34	30.33 (± 1.354)	30 (± 2.035)		
Week 25, 4 weeks post last dose, n=40, 32	30.41 (± 1.196)	30.26 (± 1.243)		

Notes:

[35] - Safety Population

[36] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of the hematology parameter of mean corpuscular volume (MCV) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute values of the hematology parameter of mean corpuscular volume (MCV) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

MCV was assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[37]	51 ^[38]		
Units: Femtoliters				
arithmetic mean (standard deviation)				
Week 1, pre-dose, n=52, 52	90.04 (± 3.85)	89.43 (± 5.051)		
Week 2, n=53, 52	90.06 (± 3.997)	89.41 (± 4.765)		
Week 5, pre-dose, n=53, 50	89.85 (± 3.911)	89.38 (± 4.876)		
Week 9, pre-dose, n=51, 46	89.81 (± 3.897)	89.07 (± 5.019)		
Week 13, pre-dose, n=45, 40	89.19 (± 3.934)	89.12 (± 5.358)		
Week 17, pre-dose, n=45, 35	89.5 (± 3.714)	89.33 (± 5.469)		
Week 21, pre-dose, n=42, 34	89.46 (± 3.673)	89.23 (± 5.542)		
Week 25, 4 weeks post last dose, n=41, 32	89.68 (± 3.364)	89.91 (± 3.831)		

Notes:

[37] - Safety Population

[38] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute value of the hematology parameter of reticulocyte count/erythrocyte uncorrected at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Absolute value of the hematology parameter of reticulocyte count/erythrocyte uncorrected at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Reticulocyte count was assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 ^[39]	16 ^[40]		
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Week 1, pre-dose, n=19, 16	0.1723 (± 0.16091)	0.1053 (± 0.0575)		
Week 2, n=19, 16	0.171 (± 0.15032)	0.1271 (± 0.09305)		
Week 5, pre-dose, n=19, 16	0.1731 (± 0.16016)	0.1464 (± 0.13471)		

Week 9, pre-dose, n=18, 16	0.1556 (± 0.12224)	0.1299 (± 0.10015)		
Week 13, pre-dose, n=15, 16	0.1483 (± 0.12563)	0.1324 (± 0.10103)		
Week 17, pre-dose, n=15, 14	0.1645 (± 0.17438)	0.1423 (± 0.13603)		
Week 21, pre-dose, n=15, 13	0.1446 (± 0.1135)	0.1395 (± 0.11754)		
Week 25, 4 weeks post last dose, n=15, 12	0.1465 (± 0.12045)	0.1402 (± 0.0966)		

Notes:

[39] - Safety Population

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive urinalysis results at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Number of participants with positive urinalysis results at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
End point description:	
Specific gravity, power of hydrogen (pH), glucose, protein, blood, and ketones were assessed at Weeks 1, 2, 5, 9, 13, 17, 21, and 25. Data was not summarized for this outcome measure.	
End point type	Secondary
End point timeframe:	
Weeks 1, 2, 5, 9, 13, 17, 21, and 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[41]	0 ^[42]		
Units: participants				

Notes:

[41] - Safety Population

[42] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse event (AE) and serious adverse event (SAE)

End point title	Number of participants with any treatment-emergent adverse event (AE) and serious adverse event (SAE)
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, is an important medical event that jeopardizes the participants or may

require medical or surgical intervention to prevent one of the other outcomes listed in the above definition, or is associated with liver injury and impaired liver function.

End point type	Secondary
End point timeframe:	
Up to Week 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[43]	51 ^[44]		
Units: participants				
Any AE	41	42		
Any SAE	0	0		

Notes:

[43] - Safety Population

[44] - Safety Population. Due to a system limitation, n=51 (ITT Pop.) is shown for this arm; however, n=52.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of the forced expiratory volume in 1 second (FEV1) at Weeks 2, 5, 9, 13, 17, 21, and 25

End point title	Mean of the forced expiratory volume in 1 second (FEV1) at Weeks 2, 5, 9, 13, 17, 21, and 25
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End point description:

FEV1 is defined as the volume of air forcefully expelled from the lungs in one second. FEV1 measurements were taken by spirometry at each clinic visit. FEV1 was calculated as the maximum of three readings taken at each time point for each participant. Spirometry data is plotted and analyzed using a repeated measures model to calculate treatment difference, confidence intervals and p-values. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
End point timeframe:	
Weeks 2, 5, 9, 13, 17, 21, and 25	

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[45]	51 ^[46]		
Units: Liters (L)				
least squares mean (confidence interval 95%)				
Week 2, n=54, 51	3.24 (3.14 to 3.35)	3.2 (3.1 to 3.31)		
Week 5, n=54, 49	3.33 (3.23 to 3.44)	3.28 (3.17 to 3.39)		
Week 9, n=47, 44	3.32 (3.19 to 3.45)	3.23 (3.09 to 3.37)		
Week 13, n=44, 37	3.35 (3.23 to 3.47)	3.18 (3.06 to 3.31)		

Week 17, n=43, 34	3.33 (3.18 to 3.48)	3.12 (2.96 to 3.28)		
Week 21, n=42, 32	3.41 (3.27 to 3.54)	3.18 (3.04 to 3.33)		
Week 25, n=42, 32	3.35 (3.23 to 3.47)	3.18 (3.05 to 3.32)		

Notes:

[45] - ITT Population: all randomized participants who received at least one dose of study treatment

[46] - ITT Population: all randomized participants who received at least one dose of study treatment

Statistical analyses

Statistical analysis title	Week 2
Comparison groups	Placebo v Mepolizumab 750 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[47]
P-value	= 0.567
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.19

Notes:

[47] - repeated measures model

Statistical analysis title	Week 5
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[48]
P-value	= 0.495
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.21

Notes:

[48] - repeated measures model

Statistical analysis title	Week 9
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[49]
P-value	= 0.365
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.28

Notes:

[49] - repeated measures model

Statistical analysis title	Week 13
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[50]
P-value	= 0.058
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.34

Notes:

[50] - repeated measures model

Statistical analysis title	Week 17
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[51]
P-value	= 0.056
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.43

Notes:

[51] - repeated measures model

Statistical analysis title	Week 21
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Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[52]
P-value	= 0.028
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.42

Notes:

[52] - repeated measures model

Statistical analysis title	Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[53]
P-value	= 0.077
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.34

Notes:

[53] - repeated measures model

Secondary: Mean of forced vital capacity (FVC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Mean of forced vital capacity (FVC) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

FVC is defined as the maximum amount of air that can forcibly be blown out after a maximum inspiration. FVC was calculated as the maximum of three readings taken at each time point for each participant. Spirometry data are plotted and analyzed using a repeated measures model to calculate treatment difference, confidence intervals and p-values. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[54]	51 ^[55]		
Units: Liters				
least squares mean (confidence interval 95%)				
Week 2, n=54, 51	4.51 (4.39 to 4.62)	4.45 (4.34 to 4.56)		
Week 5, n=54, 49	4.55 (4.45 to 4.66)	4.49 (4.38 to 4.6)		
Week 9, n=47, 44	4.52 (4.38 to 4.66)	4.46 (4.32 to 4.6)		
Week 13, n=44, 37	4.62 (4.49 to 4.75)	4.43 (4.28 to 4.57)		
Week 17, n=43, 34	4.59 (4.43 to 4.74)	4.37 (4.19 to 4.54)		
Week 21, n=42, 32	4.66 (4.51 to 4.81)	4.38 (4.22 to 4.55)		
Week 25, n=42, 32	4.59 (4.45 to 4.74)	4.41 (4.25 to 4.57)		

Notes:

[54] - ITT Population

[55] - ITT Population

Statistical analyses

Statistical analysis title	Week 2
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[56]
P-value	= 0.486
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.22

Notes:

[56] - repeated measures model

Statistical analysis title	Week 5
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[57]
P-value	= 0.384
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.22

Notes:

[57] - repeated measures model

Statistical analysis title	Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[58]
P-value	= 0.546
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.26

Notes:

[58] - repeated measures model

Statistical analysis title	Week 13
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[59]
P-value	= 0.05
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.39

Notes:

[59] - repeated measures model

Statistical analysis title	Week 17
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[60]
P-value	= 0.061
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.45

Notes:

[60] - repeated measures model

Statistical analysis title	Week 21
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[61]
P-value	= 0.016
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.51

Notes:

[61] - repeated measures model

Statistical analysis title	Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[62]
P-value	= 0.094
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.4

Notes:

[62] - repeated measures model

Secondary: Mean peak expiratory flow rate (PEFR) at indicated Weeks 1, 2, 5, 9, 13,

17, 21, and 25

End point title	Mean peak expiratory flow rate (PEFR) at indicated Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

PEFR is defined as the maximum airflow generated during a forced expiration beginning with the lungs fully inflated. PEFR was calculated as the maximum of three readings taken at each time point for each participant. Spirometry data is plotted and analyzed using a repeated measures model to calculate treatment difference, confidence intervals and p-values. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[63]	51 ^[64]		
Units: Liters/minute (L/min)				
least squares mean (confidence interval 95%)				
Week 2, n=54, 51	481.05 (462.19 to 511.95)	467.7 (449.78 to 485.63)		
Week 5, n=54, 49	472.81 (455.37 to 490.25)	474.53 (453.61 to 495.45)		
Week 9, n=47, 45	489.08 (469.08 to 509.07)	478.16 (452.57 to 503.75)		
Week 13, n=44, 37	487.07 (470.85 to 517.23)	470.81 (445.97 to 495.65)		
Week 17, n=43, 34	494.04 (467.67 to 519.69)	455.52 (427.15 to 483.89)		
Week 21, n=42, 32	493.68 (476.83 to 526.93)	463.17 (435.53 to 490.81)		
Week 25, n=42, 32	501.88 (454.31 to 507.79)	466.93 (437.33 to 496.52)		

Notes:

[63] - ITT Population

[64] - ITT Population

Statistical analyses

Statistical analysis title	Week 2
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[65]
P-value	= 0.686
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	5.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.91
upper limit	30.12

Notes:

[65] - repeated measures model

Statistical analysis title	Week 5
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[66]
P-value	= 0.321
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	14.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	43.5

Notes:

[66] - repeated measures model

Statistical analysis title	Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[67]
P-value	= 0.622
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	8.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.79
upper limit	44.6

Notes:

[67] - repeated measures model

Statistical analysis title	Week 13
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Comparison groups	Placebo v Mepolizumab 750 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[68]
P-value	= 0.178
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	23.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.75
upper limit	57.22

Notes:

[68] - repeated measures model

Statistical analysis title	Week 17
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[69]
P-value	= 0.052
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	38.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	76.66

Notes:

[69] - repeated measures model

Statistical analysis title	Week 21
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[70]
P-value	= 0.042
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	38.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	76.02

Notes:

[70] - repeated measures model

Statistical analysis title	Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[71]
P-value	= 0.484
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	14.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.76
upper limit	54.02

Notes:

[71] - repeated measures model

Secondary: Individual symptoms visual analogue scale (VAS) scores at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Individual symptoms visual analogue scale (VAS) scores at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Participants were asked to indicate on a VAS (0 to 10 centimeters) the severity of four nasal polyposis symptoms (one VAS for each symptom): rhinorrhea; mucus in the throat; nasal blockage; loss of smell. The left-hand side of the scale (0) represents "not troublesome," and the right hand side of the scale (10) represents "worst possible troublesome." Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49 ^[72]	51 ^[73]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Nasal Polyposis, Week 1, n=49, 51	8.51 (± 0.928)	8.64 (± 1.101)		
Nasal Polyposis, Week 2, n=49, 51	7.91 (± 1.766)	8.47 (± 1.326)		
Nasal Polyposis, Week 5, n=49, 49	7.1 (± 2.31)	7.75 (± 2.083)		
Nasal Polyposis, Week 9, n=47, 46	6.14 (± 3.022)	7.74 (± 2.112)		
Nasal Polyposis, Week 13, n=45, 39	5.79 (± 3.524)	7.21 (± 2.563)		
Nasal Polyposis, Week 17, n=44, 34	5 (± 3.518)	6.44 (± 3.164)		
Nasal Polyposis, Week 21, n=42, 33	4.7 (± 3.513)	6.47 (± 3.098)		
Nasal Polyposis, Week 25, n=41, 31	4.18 (± 3.624)	6.21 (± 3.357)		
Rhinorrhea, Week 1, n=49, 51	6.6 (± 2.694)	6.17 (± 3.086)		
Rhinorrhea, Week 2, n=49, 51	5.59 (± 2.863)	6.28 (± 2.992)		
Rhinorrhea, Week 5, n=49, 49	4.98 (± 3.365)	5.98 (± 2.926)		
Rhinorrhea, Week 9, n=48, 46	4.65 (± 3.309)	6.28 (± 3.129)		
Rhinorrhea, Week 13, n=45, 39	4.18 (± 3.34)	5.19 (± 3.106)		

Rhinorrhea, Week 17, n=44, 34	3.33 (± 3.338)	4.82 (± 3.399)		
Rhinorrhea, Week 21, n=42, 34	3.5 (± 3.408)	4.7 (± 3.512)		
Rhinorrhea, Week 25, n=41, 31	3.09 (± 3.452)	4.71 (± 3.812)		
Mucus in Throat, Week 1, n=49, 51	5.92 (± 2.878)	6.53 (± 2.732)		
Mucus in Throat, Week 2, n=49, 51	5.27 (± 2.807)	6.15 (± 2.764)		
Mucus in Throat, Week 5, n=49, 49	4.92 (± 3.012)	5.92 (± 2.64)		
Mucus in Throat, Week 9, n=48, 46	3.93 (± 3.232)	6.37 (± 2.942)		
Mucus in Throat, Week 13, n=45, 39	4.11 (± 3.079)	5.49 (± 3.28)		
Mucus in Throat, Week 17, n=44, 34	3.28 (± 3.19)	5.16 (± 3.482)		
Mucus in Throat, Week 21, n=42, 34	3.3 (± 3.356)	4.84 (± 3.457)		
Mucus in Throat, Week 25, n=41, 31	3.27 (± 3.298)	5.23 (± 3.405)		
Nasal Blockage, Week 1, n=49, 51	7.76 (± 2.459)	8.36 (± 1.783)		
Nasal Blockage, Week 2, n=49, 51	6.41 (± 3.02)	7.84 (± 2.466)		
Nasal Blockage, Week 5, n=49, 49	5.66 (± 3.169)	7.33 (± 2.489)		
Nasal Blockage, Week 9, n=48, 46	5.03 (± 3.387)	7.22 (± 2.959)		
Nasal Blockage, Week 13, n=45, 39	4.66 (± 3.729)	6.27 (± 3.268)		
Nasal Blockage, Week 17, n=44, 34	4.18 (± 3.556)	5.71 (± 3.597)		
Nasal Blockage, Week 21, n=42, 34	4.04 (± 3.563)	5.77 (± 3.397)		
Nasal Blockage, Week 25, n=41, 31	3.69 (± 3.476)	5.81 (± 3.494)		
Loss of Smell, Week 1, n=49, 51	9.03 (± 1.739)	9.22 (± 1.912)		
Loss of Smell, Week 2, n=49, 51	8.79 (± 1.823)	9.02 (± 1.942)		
Loss of Smell, Week 5, n=49, 49	8.28 (± 2.243)	8.69 (± 2.511)		
Loss of Smell, Week 9, n=48, 46	7.43 (± 3.192)	8.67 (± 2.647)		
Loss of Smell, Week 13, n=45, 39	7.42 (± 3.296)	8.59 (± 2.318)		
Loss of Smell, Week 17, n=44, 34	6.85 (± 3.648)	8.18 (± 2.682)		
Loss of Smell, Week 21, n=42, 34	6.74 (± 3.562)	8.2 (± 2.835)		
Loss of Smell, Week 25, n=41, 31	6.09 (± 4.089)	7.9 (± 3.378)		

Notes:

[72] - PP Population

[73] - PP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean peak nasal inspiratory flow (PNIF) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Mean peak nasal inspiratory flow (PNIF) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Participants used a portable hand-held inspiratory flow meter to measure and record PNIF in the morning prior to taking the study medication. Three measurements were taken, and the largest measurement was recorded in the electronic diary. PNIF data is plotted and analyzed using a repeated measures model to calculate treatment difference, confidence intervals and p-values. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[74]	51 ^[75]		
Units: L/min				
least squares mean (confidence interval 95%)				
Week 2, n=54, 51	120.82 (110.59 to 131.04)	99.66 (89.14 to 110.18)		
Week 5, n=54, 49	127.21 (116.76 to 137.66)	110.32 (99.39 to 121.24)		
Week 9, n=47, 46	123.91 (110.4 to 137.77)	116.71 (102.52 to 130.9)		
Week 13, n=45, 37	137.5 (123.49 to 151.51)	109.79 (94.8 to 124.78)		
Week 17, n=44, 34	132.41 (119.4 to 145.43)	117.02 (102.91 to 131.12)		
Week 21, n=42, 33	143.03 (127.13 to 158.93)	113.52 (96.28 to 130.76)		
Week 25, n=42, 32	137.02 (121.17 to 152.87)	110.37 (92.94 to 127.8)		

Notes:

[74] - ITT Population

[75] - ITT Population

Statistical analyses

Statistical analysis title	Week 2
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[76]
P-value	= 0.005
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	21.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.49
upper limit	35.83

Notes:

[76] - repeated measures model

Statistical analysis title	Week 5
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[77]
P-value	= 0.029
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	16.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	32.01

Notes:

[77] - repeated measures model

Statistical analysis title	Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[78]
P-value	= 0.472
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.64
upper limit	27.03

Notes:

[78] - repeated measures model

Statistical analysis title	Week 13
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[79]
P-value	= 0.009
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	27.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.19
upper limit	48.23

Notes:

[79] - repeated measures model

Statistical analysis title	Week 17
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Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[80]
P-value	= 0.114
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	34.59

Notes:

[80] - repeated measures model

Statistical analysis title	Week 21
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[81]
P-value	= 0.014
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	29.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.06
upper limit	52.96

Notes:

[81] - repeated measures model

Statistical analysis title	Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[82]
P-value	= 0.027
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	26.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	50.21

Notes:

[82] - repeated measures model

Secondary: Olfaction testing: worst nostril score (WNS) and mean nostril score (MNS) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point title	Olfaction testing: worst nostril score (WNS) and mean nostril score (MNS) at Weeks 1, 2, 5, 9, 13, 17, 21, and 25
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End point description:

Sniffin'Sticks were used to assess each participant's sense of smell (olfaction). Olfaction testing results were recorded for both the right and left nostrils. The worst nostril score (number of correct answers for the worst nostril) and the mean nostril score (mean number of correct answers across both nostrils) were recorded. Scores range from 0 to 12 (high score indicating normal olfactory sensation). Olfaction data are plotted and analyzed using a repeated measures model to calculate treatment difference, confidence intervals and p-values. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 5, 9, 13, 17, 21, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[83]	51 ^[84]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
MNS, Week 2, n=54, 51	3.78 (3.29 to 4.26)	3.68 (3.18 to 4.18)		
MNS, Week 5, n=54, 49	4.2 (3.63 to 4.78)	3.07 (2.46 to 3.67)		
MNS, Week 9, n=47, 45	4.48 (3.89 to 5.07)	3.69 (3.08 to 4.29)		
MNS, Week 13, n=45, 37	4.39 (3.75 to 5.03)	3.66 (2.97 to 4.35)		
MNS, Week 17, n=43, 34	4.64 (3.93 to 5.36)	4.26 (3.45 to 5.07)		
MNS, Week 21, n=42, 33	4.77 (3.93 to 5.61)	4.12 (3.19 to 5.05)		
MNS, Week 25, n=41, 32	4.4 (3.61 to 5.18)	3.69 (2.81 to 4.56)		
WNS, Week 2, n=54, 51	3.18 (2.67 to 3.69)	2.89 (2.37 to 3.42)		
WNS, Week 5, n=54, 49	3.72 (3.16 to 4.27)	2.41 (1.82 to 2.99)		
WNS, Week 9, n=47, 45	3.85 (3.21 to 4.49)	3.17 (2.51 to 3.82)		
WNS, Week 13, n=45, 37	3.76 (3.06 to 4.46)	3.14 (2.38 to 3.9)		
WNS, Week 17, n=43, 34	3.93 (3.15 to 4.7)	3.74 (2.87 to 4.61)		
WNS, Week 21, n=42, 33	4.16 (3.3 to 5.02)	3.52 (2.58 to 4.47)		
WNS, Week 25, n=41, 32	3.75 (2.93 to 4.56)	3.3 (2.4 to 4.2)		

Notes:

[83] - ITT Population

[84] - ITT Population

Statistical analyses

Statistical analysis title	MNS, Week 2
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[85]
P-value	= 0.79
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.79

Notes:

[85] - repeated measures model

Statistical analysis title	MNS, Week 5
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[86]
P-value	= 0.008
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.97

Notes:

[86] - repeated measures model

Statistical analysis title	MNS, Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[87]
P-value	= 0.066
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	1.64

Notes:

[87] - repeated measures model

Statistical analysis title	MNS, Week 13
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[88]
P-value	= 0.127
Method	repeated measures model
Parameter estimate	repeated measures model
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	1.67

Notes:

[88] - repeated measures model

Statistical analysis title	MNS, Week 17
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[89]
P-value	= 0.481
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	1.46

Notes:

[89] - repeated measures model

Statistical analysis title	MNS, Week 21
Comparison groups	Placebo v Mepolizumab 750 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[90]
P-value	= 0.308
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	1.9

Notes:

[90] - repeated measures model

Statistical analysis title	MNS, Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[91]
P-value	= 0.233
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	1.88

Notes:

[91] - repeated measures model

Statistical analysis title	WNS, Week 2
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[92]
P-value	= 0.444
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	1.02

Notes:

[92] - repeated measures model

Statistical analysis title	WNS, Week 5
Comparison groups	Mepolizumab 750 mg v Placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[93]
P-value	= 0.002
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.12

Notes:

[93] - repeated measures model

Statistical analysis title	WNS, Week 9
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[94]
P-value	= 0.143
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	1.6

Notes:

[94] - repeated measures model

Statistical analysis title	WNS, Week 13
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[95]
P-value	= 0.24
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	1.65

Notes:

[95] - repeated measures model

Statistical analysis title	WNS, Week 17
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Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[96]
P-value	= 0.75
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	1.35

Notes:

[96] - repeated measures model

Statistical analysis title	WNS, Week 21
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[97]
P-value	= 0.324
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	1.91

Notes:

[97] - repeated measures model

Statistical analysis title	WNS, Week 25
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[98]
P-value	= 0.468
Method	repeated measures model
Parameter estimate	Mean difference (final values)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	1.66

Notes:

[98] - repeated measures model

Secondary: Sino-Nasal Outcome Test (SNOT)-22 questionnaire total score at Week 1 and Week 25

End point title	Sino-Nasal Outcome Test (SNOT)-22 questionnaire total score at Week 1 and Week 25
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End point description:

The SNOT-22 questionnaire is a modification of the SNOT-20 and contains the questions related to smell and nasal obstruction. Each question is graded with a numerical score for each response; scores range from 0 for "no symptoms" to 5 for "as bad as things could be." The scores for each of the questions is summed to derive the total score for that participant at that visit. If the participant did not complete any questions at a visit, then he/she were not to have any missing values imputed, and his/her total score for that visit was set to missing. If a participant had some missing scores (but no more than 50% missing at that visit), then scores for the missing responses were imputed as the mean of the non-missing responses for that participant at that visit. The SNOT-22 total score ranges from 0 to 110, with higher scores representing a worse quality of life. Questionnaire data analysis was done using an ANCOVA to obtain the LS-means, treatment difference and confidence interval.

End point type	Secondary
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End point timeframe:

Week 1 and Week 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[99]	51 ^[100]		
Units: Scores on a scale				
least squares mean (standard error)	27.13 (± 2.96)	40.36 (± 3.39)		

Notes:

[99] - ITT Population

[100] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[101]
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mixed effects model
Point estimate	-13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.2
upper limit	-4.22

Notes:

[101] - ANCOVA model

Secondary: Index score of the EuroQoL Quality of Life-5D (EQ-5D) questionnaire at Week 1 and Week 25

End point title	Index score of the EuroQoL Quality of Life-5D (EQ-5D) questionnaire at Week 1 and Week 25
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End point description:

The EQ-5D is a standardized, 2-part questionnaire used to measure health outcomes. The first part contains descriptions of the following five components: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses to each of the five domains are measured on a 3-point scale (1-no problems, 2-some problems, and 3-severe problems). An index for the descriptive scores was derived using the general European weights, obtained for each of the countries in this study. Index scores were derived for each participant at each time point. ANCOVA model with treatment, Baseline and country as factors was used to calculate treatment difference and confidence intervals.

End point type	Secondary
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End point timeframe:

Week 1 and Week 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[102]	51 ^[103]		
Units: Scores on a scale				
least squares mean (standard error)	0.91 (± 0.02)	0.91 (± 0.02)		

Notes:

[102] - ITT Population

[103] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[104]
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.07

Notes:

[104] - ANCOVA model

Secondary: VAS score of the EQ-5D questionnaire at Week 1 and Week 25

End point title	VAS score of the EQ-5D questionnaire at Week 1 and Week 25
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End point description:

The EQ-5D is a standardized, 2-part questionnaire used to measure health outcomes. The second part of the questionnaire is a VAS question, requiring the participant to self rate his/her health score on a scale of 0 (worst imaginable health state) to 100 (best imaginable health state).

End point type	Secondary
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End point timeframe:

Week 1 and Week 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54 ^[105]	51 ^[106]		
Units: Scores on a scale				
least squares mean (standard error)	81.13 (± 2.3)	75.45 (± 2.64)		

Notes:

[105] - ITT Population

[106] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Mepolizumab 750 mg v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other ^[107]
Parameter estimate	Mean difference (final values)
Point estimate	5.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	12.68

Notes:

[107] - ANCOVA model

Secondary: Number of participants with positive immunogenicity (anti-mepolizumab antibody testing)

End point title	Number of participants with positive immunogenicity (anti-mepolizumab antibody testing)
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End point description:

Blood samples were collected at Weeks 1, 5, 13, and 25 for anti-mepolizumab antibody testing. Only those participants available at the specified time points (represented by n=X, X) were analyzed.

End point type	Secondary
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End point timeframe:

Weeks 1, 5, 13, and 25

End point values	Mepolizumab 750 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[108]	51 ^[109]		
Units: participants				
Week 1, pre-dose, n=53, 52	0	2		
Week 5, pre-dose, n=53, 50	0	2		
Week 13, pre-dose, n=45, 40	0	2		

Week 13, 4-6 months, n=1, 4	0	1		
Week 25, 4-6 months, n=25, 24	0	1		
Week 25, study exit, n=2, 2	0	1		

Notes:

[108] - ITT Population

[109] - ITT Population; n=52

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the first dose of flixonase administration (at the start of the Run-in Period) up to the end of the study (up to 11 months).

Adverse event reporting additional description:

SAEs and non-serious AEs were collected in members of the Safety Population, comprised of all enrolled participants who received at least one dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Mepolizumab 750 mg
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Reporting group description:

Participants received a total of six doses (one every 4 weeks) of mepolizumab 750 milligrams (mg) by intravenous infusion.

Reporting group title	Placebo
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Reporting group description:

Participants received a total of six doses (one every 4 weeks) of matching placebo by intravenous infusion.

Serious adverse events	Mepolizumab 750 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	0 / 52 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Mepolizumab 750 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 53 (66.04%)	39 / 52 (75.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 53 (24.53%)	22 / 52 (42.31%)	
occurrences (all)	55	35	
Sinus headache			

subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	3 / 52 (5.77%) 5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 53 (1.89%)	5 / 52 (9.62%)	
occurrences (all)	1	9	
Pyrexia			
subjects affected / exposed	3 / 53 (5.66%)	1 / 52 (1.92%)	
occurrences (all)	3	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 53 (1.89%)	6 / 52 (11.54%)	
occurrences (all)	2	8	
Otorrhoea			
subjects affected / exposed	3 / 53 (5.66%)	0 / 52 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 53 (3.77%)	4 / 52 (7.69%)	
occurrences (all)	8	6	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 53 (3.77%)	3 / 52 (5.77%)	
occurrences (all)	3	3	
Cough			
subjects affected / exposed	2 / 53 (3.77%)	3 / 52 (5.77%)	
occurrences (all)	2	3	
Dyspnoea			
subjects affected / exposed	2 / 53 (3.77%)	4 / 52 (7.69%)	
occurrences (all)	2	5	
Epistaxis			
subjects affected / exposed	1 / 53 (1.89%)	4 / 52 (7.69%)	
occurrences (all)	6	6	
Rhinorrhoea			
subjects affected / exposed	0 / 53 (0.00%)	3 / 52 (5.77%)	
occurrences (all)	0	3	

Paranasal sinus discomfort subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	3 / 52 (5.77%) 7	
Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 6	4 / 52 (7.69%) 4	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 8	0 / 52 (0.00%) 0	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	3 / 52 (5.77%) 5	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 5 5 / 53 (9.43%) 6	3 / 52 (5.77%) 4 0 / 52 (0.00%) 0	
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4 10 / 53 (18.87%) 12	2 / 52 (3.85%) 2 14 / 52 (26.92%) 17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2009	Amendment made to include more details surrounding dose administration and make minor protocol corrections. Changes and rationale described in Appendix 6.
11 November 2009	Amendment made to include revisions to the eligibility criteria relating to inhaled and oral steroid use, and to clarify the Serious Adverse Event definition. Changes and rationale described in Appendix 7.
13 July 2011	Amendment made to include revisions to the prohibited medications relating to leukotriene modifiers including montelukast and to make clarifications to the Time and Events table. Changes and rationale are described in Appendix 8.
09 November 2011	Amendment made to correct the inconsistency for the timing of the final immunogenicity sampling and the final laboratory and pregnancy testing. Changes and rationale are described in Appendix 9.
23 January 2012	Amendment made to remove Part B of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Safety Population (SP): actual treatment; Intent-to-Treat Population (ITTP): intended treatment. A placebo-randomized participant took mepolizumab; placebo SP "N" is greater than ITTP "N." Due to system limitations, SP n=51 is shown (should be n=52).

Notes: