Clinical trial results:
A Double-blind, Randomised, Placebo-controlled Study to Investigate the Efficacy and Safety of Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis in Subjects Receiving Standard of Care Therapy.

Summary

EudraCT number	2012-004385-17
Trial protocol	BE DE GB IT ES
Global end of trial date	05 September 2016

Results information

Result version number	v3
This version publication date	31 December 2017
First version publication date	14 September 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115921

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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000069-PIP04-13
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 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of mepolizumab plus standard of care compared with placebo plus standard of care on duration of clinical remission, defined as accrued duration in weeks where a subject achieves a BVAS=0 and corticosteroid dose ≤4 mg/day prednisolone/prednisone, in subjects with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) receiving standard of care therapy including corticosteroid therapy reduction/withdrawal.

To investigate the durability of response to treatment with mepolizumab plus standard of care compared with placebo plus standard of care, assessed by the proportion of subjects in remission at both Weeks 36 and 48.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2014
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	Belgium: 3
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	United States: 59
Worldwide total number of subjects	136
EEA total number of subjects	65

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)	119
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants at screening and run-in visit, entered a 52 week study treatment phase followed by 8-week follow-up phase. The total duration for the study participation was approximately 64 weeks.

Pre-assignment

Screening details:

A total of 151 participants with a history of relapsing or refractory Eosinophilic Granulomatosis with Polyangiitis (EGPA) were screened, out of which 4 were screen failures and 11 were run-in failures. 136 participants completed run-in period and received Mepolizumab 300 milligram (mg) or placebo in a randomized manner in the treatment phase.

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	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo injection via subcutaneous (SC) route once every 4 weeks along with standard of care (SOC) drugs up to Week 48.

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

Dosage and administration details:

Randomized participants received placebo (0.9 percent sodium chloride) injection via subcutaneous route once every 4 weeks along with standard of care treatment.

Arm title	Mepolizumab 300mg

Arm description:

Participants received Mepolizumab 300mg injection via SC route once every 4 weeks along with SOC drugs up to Week 48.

Arm type	Experimental
Investigational medicinal product name	Mepolizumab 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Randomized participants received Mepolizumab 300 mg injection via subcutaneous route once every 4 weeks along with standard of care treatment.

Number of subjects in period 1	Placebo	Mepolizumab 300mg
Started	68	68
Completed	61	65
Not completed	7	3
Adverse event, serious fatal	-	1
Physician decision	2	-
Consent withdrawn by subject	3	2
Lost to follow-up	1	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo injection via subcutaneous (SC) route once every 4 weeks along with standard of care (SOC) drugs up to Week 48.	
Reporting group title	Mepolizumab 300mg
Reporting group description:	
Participants received Mepolizumab 300mg injection via SC route once every 4 weeks along with SOC drugs up to Week 48.	

Reporting group values	Placebo	Mepolizumab 300mg	Total
Number of subjects	68	68	136
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 48.2 ± 14.32	 48.7 ± 12.39	 -
Gender categorical Units: Subjects			
Female	38	42	80
Male	30	26	56
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	1	1
Asian - Japanese Heritage	3	3	6
Asian - South East Asian Heritage	2	0	2
White - Arabic/North African Heritage	0	2	2
White - White/Caucasian/European Heritage	61	62	123
Mixed Race	2	0	2

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo injection via subcutaneous (SC) route once every 4 weeks along with standard of care (SOC) drugs up to Week 48.	
Reporting group title	Mepolizumab 300mg
Reporting group description:	
Participants received Mepolizumab 300mg injection via SC route once every 4 weeks along with SOC drugs up to Week 48.	

Primary: Number of Participants in Each Category of Accrued Duration of Remission

End point title	Number of Participants in Each Category of Accrued Duration of Remission
End point description:	
Total accrued duration of remission is the accrued number of weeks where Birmingham Vasculitis Activity Score (BVAS) =0 plus prednisolone/prednisone dose <=4 mg/day over the 52 week study treatment period was reported. The accrued duration was categorized into zero, >0 to <12 weeks, 12 to <24 weeks, 24 to <36 weeks and >=36 weeks. Statistical analysis was based on a proportional odds regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region. Intent-to-Treat (ITT) Population was used for the analysis and was defined as all participants who were randomized and received at least one dose of trial medication. Randomized participants were assumed to have received study treatment unless definitive evidence to the contrary exists. The odds ratio for treatment difference and associated probability (p)-value and 95 percent confidence interval (CI) were calculated.	
End point type	Primary
End point timeframe:	
Up to Week 52	

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[1]	68[2]		
Units: Participants				
Zero	55	32		
>0 to <12 weeks	8	8		
12 to <24 weeks	3	9		
24 to <36 weeks	0	10		
>=36 weeks	2	9		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 300mg v Placebo

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [3]
Method	Proportional odds regression model
Parameter estimate	Odds ratio (OR)
Point estimate	5.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.68
upper limit	13.03

Notes:

[3] - P- value was based on a proportional odds regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region.

Primary: Number of participants who are in remission at 36 and 48 weeks

End point title	Number of participants who are in remission at 36 and 48 weeks

End point description:

The number of participants who were in remission (i.e ., BVAS=0 and prednisolone /prednisone <=4 mg/day) at both Weeks 36 and 48 of the study treatment period was reported. The statistical analysis was performed using a logistic regression model on ITT Population. The odds ratio for treatment difference and associated p-value and 95 percent CI were calculated.

End point type	Primary

End point timeframe:

Week 36 and Week 48

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[4]	68[5]		
Units: Participants				
Participants	2	22		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 300mg v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	16.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.61
upper limit	77.56

Secondary: Time to First EGPA Relapse

End point title	Time to First EGPA Relapse

End point description:

EGPA relapse was defined as worsening or persistence of active disease since the last visit characterized by active vasculitis or active asthma symptoms and/or signs with a corresponding worsening in Asthma Control Questionnaire-6 (ACQ-6) score or active nasal and/or sinus disease, with a corresponding worsening in at least one of the sino-nasal symptom questions warranting: i) an increased dose of OCS therapy (or other systemic corticosteroid therapy) to >4 mg/day prednisolone total daily dose or equivalent; OR ii) an increased dose or addition of immunosuppressive therapy; OR iii) hospitalization related to EGPA worsening. Participants who completed study, or withdrawn prematurely from the study without experiencing the event were censored.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[6]	68[7]		
Units: Participants				
Category title 1	56	38		

Notes:

[6] - ITT Population

[7] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 300mg v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.001 [9]
Method	Cox Proportional Hazard regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.322
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.206
upper limit	0.502

Notes:

[8] - Hazard ratio (Mepolizumab 300mg/Placebo)

[9] - p-value was based on a cox proportional hazards model with covariates of treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region.

Secondary: Number of Participants in Each Category of Average Daily Prednisolone/Prednisone Dose During the Last 4 Weeks of the Study Treatment Period

End point title	Number of Participants in Each Category of Average Daily Prednisolone/Prednisone Dose During the Last 4 Weeks of the Study Treatment Period

End point description:

The number of participants with an average daily prednisolone/prednisone dose during the last 4 weeks of the Study Treatment Period (48 through 52) was calculated. The average dose was categorized into zero, >0 to <=4.0mg, >4.0 to <=7.5mg and >7.5mg. The statistical analysis was performed using a proportional odds regression model with Baseline covariates of treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region and the comparison between treatment groups was presented as an odds ratio, p-value and 95 percent CI.

End point type	Secondary

End point timeframe:

Week 48 and Week52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[10]	68[11]		
Units: Participants				
Zero	2	12		
>0 to <=4.0mg	3	18		
>4.0 to <=7.5mg	18	10		
>7.5mg	45	28		

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 300mg v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.001 [13]
Method	Proportional odds regression model
Parameter estimate	Odds ratio (OR)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.41

Notes:

[12] - Odds ratio (Mepolizumab 300mg/Placebo)

[13] - p-value was based on a proportional odds regression model with Baseline covariates of treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region.

Secondary: Number of participants who achieved remission within the first 24 weeks and remained in remission for the remainder of the treatment period

End point title	Number of participants who achieved remission within the first 24 weeks and remained in remission for the remainder of the treatment period

End point description:

The number of participants who achieved remission (i.e., BVAS=0 and prednisolone/prednisone<=4 mg/day) within the first 24 weeks and remain in remission for the remainder of the study treatment period was reported. The statistical analysis was performed using a logistic regression model on ITT Population. The odds ratio for treatment difference and associated p-value and 95 percent CI were calculated.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[14]	68[15]		
Units: Participants				
Participants	1	13		

Notes:

[14] - ITT Population

[15] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Mepolizumab 300mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	19.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	167.93

Secondary: Number of Participants in Each Category of Accrued Duration of Remission

End point title	Number of Participants in Each Category of Accrued Duration of

	Remission

End point description:

Total accrued duration of remission, i.e., the accrued number of weeks where Birmingham Vasculitis Activity Score (BVAS) =0 plus prednisolone/prednisone dose <=7.5mg/day over the 52 week study treatment period was reported. BVAS is a validated, clinician-completed tool used for the comprehensive multisystem clinical assessment of disease activity in systemic vasculitis. The duration was categorized into zero, >0 to <12 weeks, 12 to <24 weeks, 24 to <36 weeks and >=36 weeks. Statistical analysis was performed on ITT Population and was based on a proportional odds regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region. The odds ratio for treatment difference and associated p-value and 95 percent CI were calculated.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[16]	68[17]		
Units: Participants				
Zero	36	15		
>0 to <12 weeks	19	15		
12 to <24 weeks	0	7		
24 to <36 weeks	7	9		
>=36 weeks	6	22		

Notes:

[16] - ITT Population

[17] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Mepolizumab 300mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [18]
Method	Proportional odds regression model
Parameter estimate	Odds ratio (OR)
Point estimate	5.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.63
upper limit	10.74

Notes:

[18] - P- value was based on a proportional odds regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region.

Secondary: Number of participants who are in remission at 36 and 48 weeks

End point title	Number of participants who are in remission at 36 and 48 weeks

End point description:

The number of participants who were in remission (i.e ., BVAS=0 and prednisolone /prednisone <=7.5 mg/day) at both Weeks 36 and 48 of the study treatment period was reported. The statistical analysis was performed using a logistic regression model on ITT Population. The odds ratio for treatment difference and associated p-value and 95 percent CI were calculated.

End point type	Secondary

End point timeframe:

Week 36 and Week 48

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[19]	68[20]		
Units: Participants				
Participants	7	28		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Mepolizumab 300mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [21]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	19.87

Notes:

[21] - P- value was based on logistic regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region.

Secondary: Number of participants who achieved remission (BVAS=0 and prednisolone/prednisone <=7.5 mg/day) within the first 24 weeks and remained in remission for the remainder of the treatment period

End point title	Number of participants who achieved remission (BVAS=0 and prednisolone/prednisone <=7.5 mg/day) within the first 24 weeks and remained in remission for the remainder of the treatment period

End point description:

The number of participants who were in remission (i.e ., BVAS=0 and prednisolone /prednisone <=7.5mg/day) at both Weeks 36 and 48 of the study treatment period was reported. The statistical analysis was performed using a logistic regression model on ITT Population. The odds ratio for treatment difference and associated p-value and 95 percent CI were calculated.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[22]	68[23]		
Units: Participants				
Participants	2	16		

Notes:

[22] - ITT Population

[23] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Mepolizumab 300mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.35
upper limit	55.24

Secondary: Number of participants with local and systemic Adverse Events (AEs)

End point title	Number of participants with local and systemic Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs including systemic allergic and non-allergic reactions as well as local site injection-related reactions were counted throughout treatment phase and follow up phase. Systemic allergic reactions included Facial paralysis, flushing, hypersensitivity and rash pruritic. Injection related reactions were considered as systemic non-allergic reactions. Local site reactions included injection site bruising, erythema, pain and reaction. The analysis was performed on Safety Population which comprised of all participants who receive at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[24]	68[25]		
Units: Participants				
Facial paralysis	1	0		
Flushing	0	1		
Hypersensitivity	0	1		
Rash pruritic	0	1		
Injection related reactions	0	1		
Injection site bruising	0	1		
Injection site erythema	1	1		
Injection site pain	1	0		
Injection site reaction	7	9		

Notes:

[24] - Safety Population

[25] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters of alanine aminotransferase (ALT), alkaline phosphatase (Alk.phosph.), aspartate aminotransferase (AST), creatinine kinase, gamma glutamyl transaminase (GGT) and lactate dehydrogenase (dehydro) levels

End point title	Change from Baseline in clinical chemistry parameters of alanine aminotransferase (ALT), alkaline phosphatase (Alk.phosph.), aspartate aminotransferase (AST), creatinine kinase, gamma glutamyl transaminase (GGT) and lactate dehydrogenase (dehydro) levels

End point description:

Blood samples were collected to evaluate change from Baseline in ALT, Alk.phosph., AST, creatinine kinase, GGT and lactate dehydro values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[26]	68[27]		
Units: International Unit per Liter (IU/L)				
arithmetic mean (standard deviation)				
Absolute ALT; Baseline; n= 68, 68	19.9 (± 8.91)	21.3 (± 14.22)		
ALT; Week 4; n= 68, 68	0.2 (± 6.17)	-2.2 (± 8.59)		
ALT; Week 8; n= 67, 66	-0.9 (± 5.66)	-1.7 (± 10.14)		
ALT; Week 12; n= 65, 68	-0.9 (± 4.53)	-0.7 (± 12.65)		
ALT; Week 16; n= 65, 68	-0.4 (± 6.56)	-2.2 (± 9.73)		

ALT; Week 20; n= 63, 68	-0.3 (± 6.25)	-1.2 (± 12.30)		
ALT; Week 24; n= 63, 66	-1.3 (± 5.38)	-0.2 (± 15.77)		
ALT; Week 28; n= 62, 66	-0.9 (± 6.73)	-0.4 (± 13.62)		
ALT; Week 32; n= 61, 67	-0.7 (± 6.79)	-2.4 (± 11.30)		
ALT; Week 36; n= 60, 67	-0.1 (± 6.21)	-3.0 (± 11.66)		
ALT; Week 40; n= 61, 66	0.3 (± 9.01)	-2.3 (± 11.70)		
ALT; Week 44; n= 61, 66	0.9 (± 9.68)	-2.7 (± 9.51)		
ALT; Week 48; n= 61, 64	1.7 (± 9.04)	-1.6 (± 15.47)		
ALT; Week 52; n= 60, 65	1.5 (± 10.42)	-2.8 (± 12.87)		
ALT; Week 56; n= 61, 63	-0.1 (± 7.35)	-3.6 (± 12.79)		
ALT; Week 60; n= 60, 65	-0.3 (± 7.33)	-4.7 (± 14.11)		
Absolute Alk.phosph.; Baseline; n= 68, 68	61.2 (± 17.83)	60.4 (± 20.90)		
Alk.phosph.; Week 4; n= 68, 68	-0.9 (± 6.65)	-3.2 (± 10.01)		
Alk.phosph.; Week 8; n= 67, 66	-1.7 (± 9.95)	-1.7 (± 11.56)		
Alk. phosph.; Week 12; n= 65, 68	-1.9 (± 8.36)	-1.1 (± 12.99)		
Alk. phosph.; Week 16; n= 65, 68	-1.3 (± 9.35)	-1.1 (± 14.61)		
Alk. phosph.; Week 20; n= 63, 68	0.0 (± 11.24)	4.4 (± 21.90)		
Alk. phosph.; Week 24; n= 63, 66	-1.1 (± 10.65)	2.8 (± 17.64)		
Alk. phosph.; Week 28; n= 62, 66	0.2 (± 10.95)	4.9 (± 17.17)		
Alk. phosph.; Week 32; n= 61, 67	0.2 (± 11.14)	4.4 (± 15.83)		
Alk. phosph.; Week 36; n= 60, 67	0.2 (± 10.42)	4.8 (± 14.71)		
Alk. phosph.; Week 40; n= 61, 66	1.0 (± 10.08)	6.2 (± 18.43)		
Alk. phosph.; Week 44; n= 61, 66	1.1 (± 12.55)	5.1 (± 16.53)		
Alk. phosph.; Week 48; n= 61, 64	1.2 (± 11.66)	5.1 (± 17.56)		
Alk. phosph.; Week 52; n= 60, 65	0.3 (± 12.30)	2.3 (± 14.47)		
Alk. phosph.; Week 56; n= 61, 63	-0.9 (± 12.04)	1.7 (± 16.42)		
Alk. phosph.; Week 60; n= 60, 65	-1.5 (± 13.16)	1.0 (± 15.08)		
Absolute AST; Baseline; n= 68, 68	19.3 (± 6.11)	21.8 (± 10.73)		
AST; Week 4; n= 68, 68	0.0 (± 4.41)	-1.7 (± 8.61)		
AST; Week 8; n= 67, 66	-0.4 (± 4.77)	-1.0 (± 8.21)		
AST; Week 12; n= 65, 68	0.5 (± 4.41)	-0.7 (± 9.62)		
AST; Week 16; n= 65, 68	0.4 (± 5.48)	-0.6 (± 7.90)		
AST; Week 20; n= 63, 68	0.8 (± 4.66)	-0.6 (± 8.49)		
AST; Week 24; n= 63, 66	0.0 (± 4.46)	-0.4 (± 10.44)		
AST; Week 28; n= 61, 66	-0.9 (± 5.34)	-0.4 (± 10.59)		
AST; Week 32; n= 61, 67	-0.2 (± 4.91)	-1.3 (± 10.67)		
AST; Week 36; n= 60, 67	0.2 (± 4.68)	-2.2 (± 9.61)		
AST; Week 40; n= 61, 66	0.5 (± 5.51)	-1.6 (± 8.97)		
AST; Week 44; n= 61, 66	0.4 (± 5.77)	-2.4 (± 9.02)		
AST; Week 48; n= 61, 64	1.1 (± 6.86)	-2.3 (± 10.14)		
AST; Week 52; n= 60, 65	0.9 (± 6.84)	-3.0 (± 10.49)		
AST; Week 56; n= 61, 63	-0.2 (± 4.92)	-2.8 (± 10.64)		
AST; Week 60; n= 60, 65	-0.4 (± 5.24)	-3.7 (± 10.92)		
Absolute Creatinine kinase; Baseline; n= 68, 68	99.0 (± 75.99)	88.8 (± 75.18)		
Creatinine kinase; Week 4; n= 68, 68	-2.4 (± 83.23)	2.0 (± 60.92)		
Creatinine kinase; Week 8; n= 67, 66	-5.0 (± 62.41)	3.5 (± 50.48)		
Creatinine kinase; Week 12; n= 65, 68	5.4 (± 93.24)	6.1 (± 40.86)		
Creatinine kinase; Week 16; n= 65, 68	15.8 (± 125.84)	0.5 (± 49.65)		
Creatinine kinase; Week 20; n= 63, 68	1.3 (± 78.35)	6.5 (± 54.83)		
Creatinine kinase; Week 24; n= 63, 66	-0.6 (± 56.55)	6.0 (± 66.69)		

Creatinine kinase; Week 28; n= 62, 66	-15.9 (± 59.38)	6.3 (± 55.84)		
Creatinine kinase; Week 32; n= 61, 67	-13.1 (± 59.29)	0.2 (± 49.68)		
Creatinine kinase; Week 36; n= 60, 67	-12.0 (± 65.11)	4.9 (± 52.71)		
Creatinine kinase; Week 40; n= 61, 66	2.6 (± 91.89)	2.8 (± 62.74)		
Creatinine kinase; Week 44; n= 61, 66	5.8 (± 86.76)	-2.4 (± 62.13)		
Creatinine kinase; Week 48; n= 61, 64	-8.1 (± 70.09)	-2.6 (± 90.09)		
Creatinine kinase; Week 52; n= 60, 65	0.9 (± 67.51)	0.2 (± 53.45)		
Creatinine kinase; Week 56; n= 61, 63	-8.7 (± 60.58)	-0.2 (± 62.08)		
Creatinine kinase; Week 60; n= 60, 65	-10.3 (± 65.83)	0.4 (± 61.45)		
Absolute GGT; Baseline; n= 68, 68	30.8 (± 25.49)	30.1 (± 27.24)		
GGT; Week 4; n= 68, 68	0.2 (± 11.70)	-2.0 (± 9.68)		
GGT; Week 8; n= 67, 66	-1.0 (± 8.59)	-0.6 (± 17.99)		
GGT; Week 12; n= 65, 68	-2.9 (± 6.68)	-1.9 (± 18.70)		
GGT; Week 16; n= 65, 68	-2.1 (± 10.18)	-1.5 (± 21.36)		
GGT; Week 20; n= 63, 68	1.7 (± 19.02)	-1.1 (± 24.50)		
GGT; Week 24; n= 63, 66	-1.7 (± 11.83)	-3.3 (± 22.52)		
GGT; Week 28; n= 62, 66	-1.9 (± 11.71)	-3.1 (± 16.86)		
GGT; Week 32; n= 61, 67	-1.5 (± 15.77)	-3.6 (± 17.87)		
GGT; Week 36; n= 60, 67	-2.1 (± 10.64)	-4.7 (± 14.96)		
GGT; Week 40; n= 61, 66	-0.2 (± 16.05)	-0.3 (± 19.75)		
GGT; Week 44; n= 61, 66	-2.9 (± 8.26)	-2.7 (± 15.25)		
GGT; Week 48; n= 61, 64	0.9 (± 18.91)	-3.0 (± 16.51)		
GGT; Week 52; n= 60, 65	-1.6 (± 16.44)	-4.2 (± 13.53)		
GGT; Week 56; n= 61, 63	-5.0 (± 16.77)	-3.6 (± 17.02)		
GGT; Week 60; n= 60, 65	-4.8 (± 16.45)	-5.6 (± 15.37)		
Absolute Lactate dehydro; Baseline; n= 68, 68	186.5 (± 47.82)	179.6 (± 38.88)		
Lactate dehydro; Week 4; n= 68, 68	-3.6 (± 19.73)	-2.3 (± 27.80)		
Lactate dehydro; Week 8; n= 67, 66	-8.2 (± 29.91)	-5.3 (± 24.46)		
Lactate dehydro; Week 12; n= 65, 68	-2.2 (± 27.17)	-7.7 (± 25.56)		
Lactate dehydro; Week 16; n= 65, 68	-2.6 (± 32.13)	-10.6 (± 26.12)		
Lactate dehydro; Week 20; n= 63, 68	2.2 (± 26.80)	-13.7 (± 25.79)		
Lactate dehydro; Week 24; n= 63, 66	-4.3 (± 26.22)	-13.5 (± 26.99)		
Lactate dehydro; Week 28; n= 61, 66	-8.5 (± 27.77)	-15.9 (± 30.44)		
Lactate dehydro; Week 32; n= 61, 67	-8.3 (± 25.49)	-17.1 (± 24.88)		
Lactate dehydro; Week 36; n= 60, 67	-3.6 (± 36.45)	-16.2 (± 30.54)		
Lactate dehydro; Week 40; n= 61, 66	-4.5 (± 35.81)	-13.5 (± 36.31)		
Lactate dehydro; Week 44; n= 61, 66	-2.7 (± 33.40)	-17.0 (± 31.37)		
Lactate dehydro; Week 48; n= 61, 64	0.8 (± 43.82)	-19.0 (± 30.66)		
Lactate dehydro; Week 52; n= 60, 65	-0.1 (± 34.99)	-17.8 (± 33.45)		
Lactate dehydro; Week 56; n= 61, 63	-5.2 (± 32.69)	-16.0 (± 30.87)		

Lactate dehydro; Week 60; n= 60, 65	-3.5 (± 34.15)	-12.4 (± 33.23)		

Notes:

[26] - Safety Population

[27] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters of albumin and protein levels

End point title	Change from Baseline in clinical chemistry parameters of albumin and protein levels

End point description:

Blood samples were collected to evaluate change from Baseline in albumin and protein levels values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[28]	68[29]		
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
Absolute Albumin; Baseline; n= 68, 68	43.4 (± 2.45)	43.5 (± 3.01)		
Albumin; Week 4; n= 68, 68	-0.6 (± 2.25)	-0.1 (± 2.16)		
Albumin; Week 8; n= 67, 66	-0.8 (± 2.16)	-0.6 (± 2.72)		
Albumin; Week 12; n= 65, 68	-0.2 (± 2.47)	-0.4 (± 2.64)		
Albumin; Week 16; n= 65, 68	-0.6 (± 2.57)	-0.6 (± 2.54)		
Albumin; Week 20; n= 63, 68	-0.1 (± 2.35)	-0.2 (± 2.92)		
Albumin; Week 24; n= 63, 66	0.0 (± 2.80)	0.1 (± 2.72)		
Albumin; Week 28; n= 62, 66	-0.2 (± 2.67)	0.1 (± 2.67)		
Albumin; Week 32; n= 61, 67	-0.4 (± 2.71)	-0.1 (± 2.69)		
Albumin; Week 36; n= 60, 67	-0.1 (± 2.58)	0.3 (± 3.01)		
Albumin; Week 40; n= 61, 66	-0.2 (± 2.98)	0.2 (± 2.82)		
Albumin; Week 44; n= 61, 66	0.3 (± 2.95)	-0.3 (± 2.87)		
Albumin; Week 48; n= 61, 64	-0.4 (± 2.74)	-0.3 (± 2.77)		
Albumin; Week 52; n= 60, 65	-0.5 (± 2.45)	-0.3 (± 3.10)		
Albumin; Week 56; n= 61, 63	-0.7 (± 2.84)	-0.5 (± 2.88)		
Albumin; Week 60; n= 60, 65	-0.9 (± 2.55)	-0.7 (± 3.04)		
Absolute Protein; Baseline; n= 68, 68	67.7 (± 4.26)	67.3 (± 4.46)		
Protein; Week 4; n= 68, 68	-0.8 (± 3.00)	-0.5 (± 3.19)		
Protein; Week 8; n= 67, 66	-1.5 (± 2.97)	-0.9 (± 3.60)		
Protein; Week 12; n= 65, 68	-0.6 (± 3.57)	-0.6 (± 3.30)		

Protein; Week 16; n= 65, 68	-0.3 (± 3.56)	-0.8 (± 3.93)		
Protein; Week 20; n= 63, 68	0.0 (± 3.21)	0.1 (± 4.28)		
Protein; Week 24; n= 63, 66	0.2 (± 3.99)	0.0 (± 3.96)		
Protein; Week 28; n= 62, 66	-0.2 (± 4.13)	-0.1 (± 3.59)		
Protein; Week 32; n= 61, 67	-0.5 (± 4.09)	-0.4 (± 3.91)		
Protein; Week 36; n= 60, 67	-0.2 (± 3.82)	0.2 (± 4.45)		
Protein; Week 40; n= 61, 66	-0.4 (± 3.48)	0.1 (± 3.98)		
Protein; Week 44; n= 61, 66	0.4 (± 4.43)	-0.6 (± 4.19)		
Protein; Week 48; n= 61, 64	-0.5 (± 3.94)	-0.5 (± 4.29)		
Protein; Week 52; n= 60, 65	-0.3 (± 3.75)	-0.4 (± 4.08)		
Protein; week 56; n= 61, 63	-0.1 (± 4.77)	-0.5 (± 4.21)		
Protein; Week 60; n= 60, 65	-0.4 (± 5.88)	-0.7 (± 4.17)		

Notes:

[28] - Safety Population

[29] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters of direct, indirect and total bilirubin and creatinine levels

End point title	Change from Baseline in clinical chemistry parameters of direct, indirect and total bilirubin and creatinine levels

End point description:

Blood samples were collected to evaluate change from Baseline in direct, indirect and total bilirubin and creatinine values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[30]	68[31]		
Units: micromole per liter (µmol/L)				
arithmetic mean (standard deviation)				
Absolute Total bilirubin; Baseline; n= 68, 68	9.8 (± 6.14)	8.8 (± 4.10)		
Total bilirubin; week 4; n= 68, 68	-0.9 (± 4.02)	0.1 (± 3.48)		
Total bilirubin; Week 8; n= 67, 66	-1.2 (± 4.38)	0.0 (± 3.50)		
Total bilirubin; Week 12; n= 65, 68	-0.3 (± 3.01)	0.1 (± 3.27)		
Total bilirubin; Week 16; n= 65, 68	-1.1 (± 4.15)	0.0 (± 4.14)		
Total bilirubin; Week 20; n= 63, 68	-0.5 (± 2.90)	0.3 (± 3.57)		
Total bilirubin; Week 24; n= 63, 66	-0.3 (± 3.36)	0.0 (± 2.71)		
Total bilirubin; Week 28; n= 62, 66	-0.8 (± 3.13)	0.3 (± 4.43)		
Total bilirubin; Week 32; n= 61, 67	-1.1 (± 3.07)	-0.1 (± 3.63)		
Total bilirubin; Week 36; n= 60, 67	-0.7 (± 3.39)	0.1 (± 4.09)		

Total bilirubin; Week 40; n= 61, 66	-0.2 (± 3.22)	-0.3 (± 3.78)		
Total bilirubin; Week 44; n= 61, 66	0.0 (± 2.50)	0.1 (± 3.64)		
Total bilirubin; Week 48; n= 61, 64	-0.2 (± 2.59)	-0.1 (± 3.77)		
Total bilirubin; Week 52; n= 60, 65	-0.1 (± 3.41)	0.7 (± 3.92)		
Total bilirubin; Week 56; n= 61, 63	-0.8 (± 3.17)	0.5 (± 3.24)		
Total bilirubin; Week 60; n= 60, 65	-0.5 (± 3.21)	0.0 (± 3.42)		
Absolute Creatinine; Baseline; n= 68, 68	75.49 (± 12.878)	73.00 (± 12.289)		
Creatinine; Week 4; n= 68, 68	0.69 (± 7.195)	2.09 (± 5.533)		
Creatinine; Week 8; n= 67, 66	1.87 (± 7.505)	1.15 (± 6.737)		
Creatinine; Week 12; n= 65, 68	1.50 (± 9.029)	0.34 (± 7.006)		
Creatinine; Week 16; n= 65, 68	1.53 (± 10.012)	2.72 (± 6.702)		
Creatinine; Week 20; n= 63, 68	1.73 (± 6.916)	2.60 (± 7.739)		
Creatinine; Week 24; n= 63, 66	0.74 (± 7.775)	0.06 (± 6.538)		
Creatinine; Week 28; n= 62, 66	0.96 (± 7.504)	1.02 (± 7.764)		
Creatinine; Week 32; n= 61, 67	1.89 (± 9.809)	1.85 (± 8.589)		
Creatinine; Week 36; n= 60, 67	1.42 (± 6.957)	0.40 (± 7.839)		
Creatinine; Week 40; n= 61, 66	1.16 (± 8.253)	0.34 (± 8.119)		
Creatinine; Week 44; n= 61, 66	2.14 (± 8.991)	0.04 (± 9.070)		
Creatinine; Week 48; n= 61, 64	1.53 (± 7.972)	-2.25 (± 7.398)		
Creatinine; Week 52; n= 60, 65	0.52 (± 7.719)	-1.35 (± 7.182)		
Creatinine; Week 56; n= 61, 63	1.39 (± 7.367)	-0.30 (± 8.695)		
Creatinine; Week 60; n= 60, 65	0.34 (± 7.014)	-1.22 (± 10.896)		
Absolute Direct bilirubin; Baseline; n= 68, 68	2.1 (± 1.33)	1.9 (± 0.98)		
Direct bilirubin; Week 4; n= 68, 68	0.0 (± 1.06)	0.0 (± 0.84)		
Direct bilirubin; Week 8; n= 67, 66	0.0 (± 1.01)	0.1 (± 0.96)		
Direct bilirubin; Week 12; n= 65, 68	0.0 (± 0.97)	0.0 (± 1.04)		
Direct bilirubin; Week 16; n= 65, 68	-0.2 (± 0.96)	-0.1 (± 1.20)		
Direct bilirubin; Week 20; n= 63, 68	0.0 (± 0.86)	0.1 (± 1.03)		
Direct bilirubin; Week 24; n= 63, 66	0.1 (± 0.90)	0.0 (± 0.88)		
Direct bilirubin; Week 28; n= 62, 66	-0.1 (± 1.20)	0.2 (± 1.15)		
Direct bilirubin; Week 32; n= 61, 67	-0.2 (± 0.99)	0.1 (± 0.99)		
Direct bilirubin; Week 36; n= 60, 67	-0.1 (± 1.11)	0.1 (± 1.17)		
Direct bilirubin; Week 40; n= 61, 66	0.0 (± 1.11)	0.0 (± 0.94)		
Direct bilirubin; Week 44; n= 61, 66	0.1 (± 0.93)	0.0 (± 1.12)		
Direct bilirubin; Week 48; n= 61, 64	0.1 (± 0.99)	0.0 (± 1.17)		
Direct bilirubin; Week 52; n= 60, 65	0.1 (± 1.05)	0.2 (± 1.06)		
Direct bilirubin; Week 56; n= 61, 63	0.1 (± 1.08)	0.1 (± 1.06)		
Direct bilirubin; Week 60; n= 60, 65	0.1 (± 1.10)	0.1 (± 1.07)		
Absolute Indirect bilirubin; Baseline; n= 68, 68	7.7 (± 5.09)	6.9 (± 3.38)		
Indirect bilirubin; Week 4; n= 68, 68	-0.8 (± 3.68)	0.0 (± 3.06)		
Indirect bilirubin; Week 8; n= 67, 66	-1.2 (± 3.86)	-0.1 (± 2.94)		
Indirect bilirubin; Week 12; n= 65, 68	-0.3 (± 2.61)	0.1 (± 2.79)		
Indirect bilirubin; Week 16; n= 65, 68	-0.9 (± 3.67)	0.1 (± 3.37)		
Indirect bilirubin; Week 20; n= 63, 68	-0.5 (± 2.37)	0.2 (± 3.00)		
Indirect bilirubin; Week 24; n= 63, 66	-0.4 (± 2.94)	0.0 (± 2.37)		
Indirect bilirubin; Week 28; n= 62, 66	-0.7 (± 2.60)	0.1 (± 3.71)		

Indirect bilirubin; Week 32; n= 61, 66	-0.9 (± 2.48)	-0.2 (± 3.02)		
Indirect bilirubin; Week 36; n= 60, 67	-0.6 (± 2.77)	0.0 (± 3.30)		
Indirect bilirubin; Week 40; n= 61, 66	-0.1 (± 2.56)	-0.2 (± 3.16)		
Indirect bilirubin; Week 44; n= 61, 66	-0.1 (± 2.19)	0.1 (± 2.99)		
Indirect bilirubin; Week 48; n= 61, 64	-0.3 (± 2.19)	-0.1 (± 3.13)		
Indirect bilirubin; Week 52; n= 60, 65	-0.2 (± 2.84)	0.5 (± 3.32)		
Indirect bilirubin; Week 56; n= 61, 63	-0.9 (± 2.72)	0.4 (± 2.64)		
Indirect bilirubin; Week 60; n= 60, 65	-0.6 (± 2.64)	-0.1 (± 2.81)		

Notes:

[30] - Safety Population

[31] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in calcium, chloride, cholesterol, glucose, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, phosphorus, potassium, sodium, urea nitrogen and very low density lipoprotein (VLDL) cholesterol levels

End point title	Change from Baseline in calcium, chloride, cholesterol, glucose, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, phosphorus, potassium, sodium, urea nitrogen and very low density lipoprotein (VLDL) cholesterol levels

End point description:

Blood samples were collected to evaluate change from Baseline in calcium, chloride, cholesterol, glucose, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, phosphorus, potassium, sodium, urea nitrogen and very low density lipoprotein (VLDL) cholesterol values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured. 99999 indicates that data were not available.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[32]	68[33]		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Absolute Calcium; Baseline; n= 68, 68	2.365 (± 0.0864)	2.382 (± 0.1189)		
Calcium; Week 4; n= 68, 68	-0.011 (± 0.0836)	-0.012 (± 0.1200)		
Calcium; Week 8; n= 67, 66	-0.013 (± 0.0877)	-0.010 (± 0.1003)		
Calcium; Week 12; n= 65, 68	-0.013 (± 0.0844)	-0.026 (± 0.0889)		
Calcium; Week 16; n= 65, 68	0.000 (± 0.1091)	-0.029 (± 0.1018)		

Calcium; Week 20; n= 63, 68	0.002 (± 0.0882)	-0.016 (± 0.1032)		
Calcium; Week 24; n= 63, 66	0.001 (± 0.0901)	-0.013 (± 0.1111)		
Calcium; Week 28; n= 61, 66	0.001 (± 0.0962)	-0.001 (± 0.1039)		
Calcium; Week 32; n= 61, 67	0.000 (± 0.0911)	-0.006 (± 0.0977)		
Calcium; Week 36; n= 60, 67	-0.006 (± 0.0931)	-0.006 (± 0.1133)		
Calcium; Week 40; n= 61, 66	0.014 (± 0.1126)	0.005 (± 0.1115)		
Calcium; Week 44; n= 61, 66	0.016 (± 0.1144)	-0.020 (± 0.1115)		
Calcium; Week 48; n= 61, 64	-0.007 (± 0.1007)	-0.018 (± 0.1002)		
Calcium; Week 52; n= 60, 65	-0.008 (± 0.1001)	-0.027 (± 0.1110)		
Calcium; Week 56; n= 61, 63	-0.008 (± 0.0931)	-0.015 (± 0.0994)		
Calcium; Week 60; n= 60, 65	-0.025 (± 0.0946)	-0.019 (± 0.1058)		
Absolute Chloride; Baseline; n= 68, 68	103.4 (± 2.05)	104.0 (± 2.21)		
Chloride; Week 4; n= 68, 68	0.6 (± 1.97)	0.2 (± 2.00)		
Chloride; Week 8; n= 67, 66	0.9 (± 2.05)	0.5 (± 2.06)		
Chloride; Week 12; n= 65, 68	0.7 (± 2.32)	0.7 (± 2.20)		
Chloride; Week 16; n= 65, 68	0.5 (± 2.08)	0.8 (± 1.95)		
Chloride; Week 20; n= 63, 68	0.3 (± 2.38)	0.7 (± 2.04)		
Chloride; Week 24; n= 63, 66	0.6 (± 2.51)	0.8 (± 2.20)		
Chloride; Week 28; n= 62, 66	0.7 (± 2.17)	0.8 (± 2.59)		
Chloride; Week 32; n= 61, 67	0.4 (± 2.24)	0.5 (± 2.32)		
Chloride; Week 36; n= 60, 67	0.8 (± 2.53)	0.6 (± 2.08)		
Chloride; Week 40; n= 61, 66	0.9 (± 2.22)	0.7 (± 2.13)		
Chloride; Week 44; n= 61, 66	0.5 (± 2.13)	0.6 (± 2.55)		
Chloride; Week 48; n= 61, 64	0.5 (± 2.38)	0.5 (± 2.34)		
Chloride; Week 52; n= 60, 65	0.3 (± 2.26)	0.4 (± 2.24)		
Chloride; Week 56; n= 61, 63	0.7 (± 2.27)	0.2 (± 2.06)		
Chloride; Week 60; n= 60, 65	0.4 (± 2.01)	0.4 (± 2.20)		
Absolute Cholesterol; Baseline; n= 68, 68	5.771 (± 1.2033)	5.788 (± 1.2386)		
Cholesterol; Week 8; n= 2, 0	-0.250 (± 0.1414)	99999 (± 99999)		
Cholesterol; Week 12; n= 1, 0	0.050 (± 99999)	99999 (± 99999)		
Cholesterol; Week 16; n= 1, 1	-0.400 (± 99999)	-0.300 (± 99999)		
Cholesterol; Week 20; n= 1, 1	0.050 (± 99999)	-0.300 (± 99999)		
Cholesterol; Week 24; n= 0, 1	99999 (± 99999)	-0.560 (± 99999)		
Cholesterol; Week 36; n= 0, 1	99999 (± 99999)	0.420 (± 99999)		
Cholesterol; Week 52; n= 60, 65	-0.006 (± 0.9364)	-0.384 (± 0.8798)		
Cholesterol; Week 56; n= 1, 0	-0.220 (± 99999)	99999 (± 99999)		
Absolute Glucose; Baseline; n= 68, 68	5.76 (± 2.000)	5.35 (± 1.195)		
Glucose; Week 4; n= 68, 68	0.27 (± 1.619)	-0.01 (± 1.050)		

Glucose; Week 8; n= 67, 66	0.09 (± 1.695)	0.07 (± 0.986)		
Glucose; Week 12; n= 65, 68	0.27 (± 1.961)	0.26 (± 1.079)		
Glucose; Week 16; n= 65, 68	0.03 (± 1.454)	0.04 (± 1.077)		
Glucose; Week 20; n= 63, 68	0.25 (± 1.644)	-0.03 (± 1.351)		
Glucose; Week 24; n= 63, 66	0.02 (± 1.588)	0.16 (± 1.211)		
Glucose; Week 28; n= 62, 66	0.14 (± 1.613)	0.21 (± 1.551)		
Glucose; Week 32; n= 61, 67	-0.03 (± 1.808)	-0.14 (± 1.162)		
Glucose; Week 36; n= 60, 67	0.11 (± 1.525)	0.03 (± 1.003)		
Glucose; Week 40; n= 61, 66	0.34 (± 1.831)	-0.03 (± 1.305)		
Glucose; Week 44; n= 61, 66	0.21 (± 1.766)	-0.05 (± 0.891)		
Glucose; Week 48; n= 61, 64	0.32 (± 2.065)	0.21 (± 1.740)		
Glucose; Week 52; n= 60, 65	-0.17 (± 1.650)	0.02 (± 1.258)		
Glucose; Week 56; n= 61, 63	0.01 (± 1.718)	0.13 (± 1.852)		
Glucose; Week 60; n= 60, 65	0.20 (± 1.664)	0.11 (± 1.483)		
Absolute HDL cholesterol; Baseline; n= 68, 68	1.837 (± 0.4540)	1.937 (± 0.5606)		
HDL cholesterol; Week 8; n= 2, 0	-0.075 (± 0.0354)	99999 (± 99999)		
HDL cholesterol; Week 12; n= 1, 0	-0.100 (± 99999)	99999 (± 99999)		
HDL cholesterol; Week 16; n= 1, 1	0.400 (± 99999)	-0.150 (± 99999)		
HDL cholesterol; Week 20; n= 1, 1	0.000 (± 99999)	-0.250 (± 99999)		
HDL cholesterol; Week 24; n= 0, 1	99999 (± 99999)	-0.390 (± 99999)		
HDL cholesterol; Week 36; n= 0, 1	99999 (± 99999)	0.400 (± 99999)		
HDL cholesterol; Week 52; n= 60, 65	-0.045 (± 0.2832)	-0.150 (± 0.3146)		
HDL cholesterol; Week 56; n= 1, 0	-0.060 (± 99999)	99999 (± 99999)		
Absolute LDL cholesterol; Baseline; n= 67, 68	3.261 (± 1.0808)	3.205 (± 1.0992)		
LDL cholesterol; Week 8; n= 1, 0	-0.350 (± 99999)	99999 (± 99999)		
LDL cholesterol; Week 12; n= 1, 0	0.190 (± 99999)	99999 (± 99999)		
LDL cholesterol; Week 16; n= 1, 1	-0.730 (± 99999)	-0.790 (± 99999)		
LDL cholesterol; Week 20; n= 1, 1	-0.150 (± 99999)	-0.540 (± 99999)		
LDL cholesterol; Week 24; n= 0, 1	99999 (± 99999)	0.040 (± 99999)		
LDL cholesterol; Week 36; n= 0, 1	99999 (± 99999)	0.250 (± 99999)		
LDL cholesterol; Week 52; n= 58, 64	0.016 (± 0.7717)	-0.215 (± 0.8079)		
LDL cholesterol; Week 56; n= 1, 0	0.100 (± 99999)	99999 (± 99999)		
Absolute Phosphate; Baseline; n= 68, 68	1.068 (± 0.1797)	1.066 (± 0.1939)		
Phosphate; Week 4; n= 68, 68	-0.027 (± 0.2183)	0.014 (± 0.1833)		

Phosphate; Week 8; n= 67, 66	-0.004 (± 0.1577)	0.024 (± 0.2239)		
Phosphate; Week 12; n= 65, 68	0.003 (± 0.1821)	0.019 (± 0.2181)		
Phosphate; Week 16; n= 65, 68	0.016 (± 0.1819)	0.016 (± 0.2205)		
Phosphate; Week 20; n= 63, 68	-0.001 (± 0.1611)	0.019 (± 0.2087)		
Phosphate; Week 24; n= 63, 66	-0.042 (± 0.1565)	0.007 (± 0.2142)		
Phosphate; Week 28; n= 62, 66	-0.025 (± 0.1819)	0.003 (± 0.2539)		
Phosphate; Week 32; n= 61, 67	-0.018 (± 0.1975)	0.040 (± 0.2172)		
Phosphate; Week 36; n= 60, 67	-0.038 (± 0.2159)	0.023 (± 0.2260)		
Phosphate; Week 40; n= 61, 66	-0.029 (± 0.1822)	0.026 (± 0.2213)		
Phosphate; Week 44; n= 61, 66	-0.018 (± 0.2104)	0.041 (± 0.2240)		
Phosphate; Week 48; n= 61, 64	-0.053 (± 0.1931)	-0.020 (± 0.2443)		
Phosphate; Week 52; n= 60, 65	0.005 (± 0.1939)	0.053 (± 0.2988)		
Phosphate; Week 56; n= 61, 63	0.019 (± 0.2962)	0.043 (± 0.3066)		
Phosphate; Week 60; n= 60, 65	-0.035 (± 0.2125)	-0.007 (± 0.2322)		
Absolute Potassium; Baseline; n= 68, 68	4.11 (± 0.348)	4.10 (± 0.359)		
Potassium; Week 4; n= 68, 68	0.05 (± 0.378)	-0.02 (± 0.345)		
Potassium; Week 8; n= 67, 66	0.01 (± 0.309)	0.02 (± 0.323)		
Potassium; Week 12; n= 65, 68	-0.04 (± 0.318)	0.01 (± 0.296)		
Potassium; Week 16; n= 65, 68	0.06 (± 0.340)	0.05 (± 0.317)		
Potassium; Week 20; n= 63, 68	0.08 (± 0.382)	0.01 (± 0.372)		
Potassium; Week 24; n= 63, 66	-0.02 (± 0.298)	0.04 (± 0.350)		
Potassium; Week 28; n= 61, 66	0.07 (± 0.338)	0.10 (± 0.382)		
Potassium; Week 32; n= 61, 67	0.04 (± 0.340)	0.11 (± 0.305)		
Potassium; Week 36; n= 60, 67	0.02 (± 0.291)	0.01 (± 0.351)		
Potassium; Week 40; n= 61, 66	0.08 (± 0.419)	0.14 (± 0.313)		
Potassium; Week 44; n= 61, 66	0.08 (± 0.383)	0.09 (± 0.341)		
Potassium; Week 48; n= 61, 64	0.09 (± 0.367)	0.05 (± 0.349)		
Potassium; Week 52; n= 60, 65	0.05 (± 0.344)	0.01 (± 0.329)		
Potassium; Week 56; n= 61, 63	0.08 (± 0.379)	0.08 (± 0.378)		
Potassium; Week 60; n= 60, 65	0.00 (± 0.358)	0.10 (± 0.390)		
Absolute Sodium; Baseline; n= 68, 68	139.8 (± 2.03)	140.3 (± 1.83)		
Sodium; Week 4; n= 68, 68	0.2 (± 1.86)	0.3 (± 2.03)		
Sodium; Week 8; n= 67, 66	0.4 (± 2.06)	0.2 (± 1.89)		
Sodium; Week 12; n= 65, 68	0.1 (± 1.99)	-0.1 (± 2.28)		
Sodium; Week 16; n= 65, 68	0.0 (± 1.46)	-0.1 (± 1.91)		
Sodium; Week 20; n= 63, 68	0.0 (± 1.88)	0.1 (± 2.09)		
Sodium; Week 24; n= 63, 66	0.2 (± 1.94)	0.0 (± 1.95)		
Sodium; Week 28; n= 62, 66	0.5 (± 1.71)	0.0 (± 2.23)		
Sodium; Week 32; n= 61, 67	0.3 (± 1.92)	0.1 (± 2.13)		
Sodium; Week 36; n= 60, 67	0.4 (± 2.10)	0.0 (± 1.95)		

Sodium; Week 40; n= 61, 66	0.2 (± 2.42)	0.0 (± 2.18)		
Sodium; Week 44; n= 61, 66	0.1 (± 1.77)	-0.2 (± 2.02)		
Sodium; Week 48; n= 61, 64	0.1 (± 2.03)	-0.4 (± 1.97)		
Sodium; Week 52; n= 60, 65	0.4 (± 1.79)	-0.2 (± 2.17)		
Sodium; Week 56; n= 61, 63	0.4 (± 2.15)	-0.5 (± 2.08)		
Sodium; Week 60; n= 60, 65	-0.1 (± 2.04)	-0.3 (± 2.36)		
Absolute Urea; Baseline; n= 68, 68	5.94 (± 1.451)	5.79 (± 1.629)		
Urea; Week 4; n= 68, 68	-0.08 (± 1.412)	0.09 (± 1.241)		
Urea; Week 8; n= 67, 66	-0.23 (± 1.564)	0.20 (± 1.206)		
Urea; Week 12; n= 65, 68	-0.15 (± 1.414)	-0.10 (± 1.217)		
Urea; Week 16; n= 65, 68	-0.07 (± 1.569)	0.00 (± 1.317)		
Urea; Week 20; n= 63, 68	-0.21 (± 1.465)	-0.23 (± 1.286)		
Urea; Week 24; n= 63, 66	-0.28 (± 1.513)	-0.12 (± 1.172)		
Urea; Week 28; n= 62, 66	-0.21 (± 1.525)	-0.22 (± 1.350)		
Urea; Week 32; n= 61, 67	-0.11 (± 1.320)	-0.23 (± 1.359)		
Urea; Week 36; n= 60, 67	-0.27 (± 1.407)	-0.32 (± 1.391)		
Urea; Week 40; n= 61, 66	-0.44 (± 1.377)	-0.23 (± 1.375)		
Urea; Week 44; n= 61, 66	-0.32 (± 1.731)	-0.19 (± 1.698)		
Urea; Week 48; n= 61, 64	-0.36 (± 1.422)	-0.09 (± 1.429)		
Urea; Week 52; n= 60, 65	-0.19 (± 1.737)	-0.18 (± 1.128)		
Urea; Week 56; n= 61, 63	-0.11 (± 1.495)	-0.13 (± 1.539)		
Urea; Week 60; n= 60, 65	-0.09 (± 1.546)	-0.10 (± 1.170)		
Absolute VLDL cholesterol; Baseline; n= 67, 68	0.680 (± 0.2846)	0.646 (± 0.2841)		
VLDL cholesterol; Week 8; n= 1, 0	0.100 (± 99999)	99999 (± 99999)		
VLDL cholesterol; Week 12; n= 1, 0	-0.040 (± 99999)	99999 (± 99999)		
VLDL cholesterol; Week 16; n= 1, 1	-0.070 (± 99999)	0.640 (± 99999)		
VLDL cholesterol; Week 20; n= 1, 1	0.200 (± 99999)	0.490 (± 99999)		
VLDL cholesterol; Week 24; n= 0, 1	99999 (± 99999)	-0.210 (± 99999)		
VLDL cholesterol; Week 36; n= 0, 1	99999 (± 99999)	-0.230 (± 99999)		
VLDL cholesterol; Week 52; n= 58, 64	-0.019 (± 0.3229)	-0.051 (± 0.1927)		
VLDL cholesterol; Week 56; n= 1, 0	-0.260 (± 99999)	99999 (± 99999)		

Notes:

[32] - Safety Population

[33] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of troponin levels

End point title	Change from Baseline in clinical chemistry parameter of troponin levels

End point description:

Blood samples were collected to evaluate change from Baseline in troponin values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[34]	68[35]		
Units: µg/L				
arithmetic mean (standard deviation)				
Absolute Troponin; Baseline; n= 68, 68	0.013 (± 0.0110)	0.013 (± 0.0092)		
Troponin; Week 4; n= 68, 66	-0.001 (± 0.0106)	0.008 (± 0.0717)		
Troponin; Week 8; n= 67, 67	-0.002 (± 0.0111)	0.001 (± 0.0089)		
Troponin; Week 12; n= 64, 67	-0.002 (± 0.0108)	-0.001 (± 0.0053)		
Troponin; Week 16; n= 65, 68	-0.002 (± 0.0104)	0.002 (± 0.0272)		
Troponin; Week 20; n= 61, 68	-0.002 (± 0.0105)	-0.001 (± 0.0089)		
Troponin; Week 24; n= 62, 67	-0.002 (± 0.0098)	0.004 (± 0.0535)		
Troponin; Week 28; n= 63, 66	-0.003 (± 0.0102)	-0.002 (± 0.0090)		
Troponin; Week 32; n= 61, 67	-0.003 (± 0.0100)	-0.002 (± 0.0092)		
Troponin; Week 36; n= 61, 67	-0.002 (± 0.0107)	0.000 (± 0.0185)		
Troponin; Week 40; n= 61, 66	-0.001 (± 0.0117)	-0.002 (± 0.0090)		
Troponin; Week 44; n= 61, 65	0.000 (± 0.0068)	-0.001 (± 0.0095)		
Troponin; Week 48; n= 60, 65	0.017 (± 0.1479)	-0.001 (± 0.0101)		
Troponin; Week 52; n= 60, 65	-0.002 (± 0.0114)	-0.001 (± 0.0111)		
Troponin; Week 56; n= 61, 63	-0.003 (± 0.0112)	-0.002 (± 0.0086)		
Troponin; Week 60; n= 59, 65	-0.003 (± 0.0109)	-0.001 (± 0.0093)		

Notes:

[34] - Safety Population

[35] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters of basophils, eosinophil, leukocytes, lymphocytes, monocytes, neutrophils, platelets levels

End point title	Change from Baseline in hematology parameters of basophils, eosinophil, leukocytes, lymphocytes, monocytes, neutrophils, platelets levels

End point description:

Blood samples were collected to evaluate change from Baseline in basophils, eosinophils, leukocytes, lymphocytes, monocytes, neutrophils and platelet values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[36]	68[37]		
Units: 10^9 cells/L				
arithmetic mean (standard deviation)				
Absolute Basophils; Baselin; n= 68, 68	0.030 (± 0.0253)	0.028 (± 0.0236)		
Basophils; Week 4; n= 66, 66	-0.002 (± 0.0302)	-0.007 (± 0.0282)		
Basophils; Week 8; n= 65, 66	0.005 (± 0.0285)	-0.002 (± 0.0261)		
Basophils; Week 12; n= 63, 65	0.007 (± 0.0351)	-0.007 (± 0.0222)		
Basophils; Week 16; n= 64, 68	0.005 (± 0.0333)	-0.004 (± 0.0295)		
Basophils; Week 20; n= 61, 66	0.005 (± 0.0338)	-0.002 (± 0.0287)		
Basophils; Week 24; n= 61, 66	0.004 (± 0.0341)	-0.002 (± 0.0328)		
Basophils; Week 28; n= 62, 65	0.006 (± 0.0411)	-0.005 (± 0.0297)		
Basophils; Week 32; n= 61, 66	0.010 (± 0.0467)	0.002 (± 0.0355)		
Basophils; Week 36; n= 60, 66	0.009 (± 0.0321)	0.005 (± 0.0424)		
Basophils; Week 40; n= 61, 65	0.005 (± 0.0357)	-0.002 (± 0.0356)		

Basophils; Week 44; n= 59, 61	0.008 (± 0.0328)	0.000 (± 0.0296)		
Basophils; Week 48; n= 59, 64	0.003 (± 0.0408)	-0.004 (± 0.0300)		
Basophils; Week 52; n= 60, 64	0.004 (± 0.0289)	-0.003 (± 0.0284)		
Basophils; Week 56; n= 59, 61	0.009 (± 0.0381)	-0.003 (± 0.0286)		
Basophils; Week 60; n= 58, 64	0.002 (± 0.0316)	-0.006 (± 0.0248)		
Absolute Eosinophils; Baseline; n= 68, 68	0.362 (± 0.5835)	0.398 (± 0.8415)		
Eosinophils; Week 4; n= 66, 66	-0.054 (± 0.3309)	-0.339 (± 0.6794)		
Eosinophils; Week 8; n= 65, 66	0.103 (± 0.2921)	-0.370 (± 0.8092)		
Eosinophils; Week 12; n= 63, 65	0.027 (± 0.3515)	-0.364 (± 0.8407)		
Eosinophils; Week 16; n= 64, 68	0.058 (± 0.4092)	-0.355 (± 0.8280)		
Eosinophils; Week 20; n= 61, 66	0.162 (± 0.5900)	-0.347 (± 0.8266)		
Eosinophils; Week 24; n= 61, 66	0.136 (± 0.4044)	-0.364 (± 0.8211)		
Eosinophils; Week 28; n= 62, 65	0.172 (± 0.4365)	-0.360 (± 0.8258)		
Eosinophils; Week 32; n= 61, 66	0.079 (± 0.3759)	-0.347 (± 0.8310)		
Eosinophils; Week 36; n= 60, 66	0.086 (± 0.3758)	-0.347 (± 0.8388)		
Eosinophils; Week 40; n= 61, 65	0.022 (± 0.4448)	-0.358 (± 0.8396)		
Eosinophils; Week 44; n= 59, 61	0.051 (± 0.4472)	-0.365 (± 0.8604)		
Eosinophils; Week 48; n= 59, 64	0.109 (± 0.3873)	-0.364 (± 0.8540)		
Eosinophils; Week 52; n= 60, 64	0.055 (± 0.3764)	-0.341 (± 0.8456)		
Eosinophils; Week 56; n= 59, 61	0.071 (± 0.4137)	-0.351 (± 0.8624)		
Eosinophils; Week 60; n= 58, 64	0.111 (± 0.4666)	-0.302 (± 0.8352)		
Absolute Leukocytes; Baseline; n= 68, 68	9.91 (± 2.714)	9.54 (± 3.130)		
Leukocytes; Week 4; 66, 66	-0.11 (± 2.109)	-0.77 (± 2.356)		
Leukocytes; Week 8; n= 65, 66	-0.18 (± 2.562)	-0.83 (± 2.511)		
Leukocytes; Week 12; n= 63, 65	-0.53 (± 1.765)	-1.24 (± 2.716)		
Leukocytes; ; Week 16; n= 64, 68	0.01 (± 2.567)	-1.16 (± 2.827)		
Leukocytes; Week 20; n= 61, 66	-0.13 (± 2.269)	-1.43 (± 2.649)		
Leukocytes; Week 24; n= 61, 66	-0.73 (± 2.110)	-1.47 (± 2.738)		
Leukocytes; Week 28; n= 62, 65	-0.01 (± 2.297)	-1.66 (± 2.804)		
Leukocytes; week 32; n= 61, 66	-0.33 (± 2.218)	-1.54 (± 2.725)		
Leukocytes; Week 36; n= 60, 66	-0.17 (± 2.501)	-1.37 (± 2.578)		

Leukocytes; Week 40; n= 61, 65	0.17 (± 2.912)	-1.28 (± 3.284)		
Leukocytes; Week 44; n= 59, 61	0.25 (± 3.166)	-1.57 (± 2.198)		
Leukocytes; Week 48; n= 59, 64	-0.10 (± 3.092)	-1.46 (± 2.546)		
Leukocytes; Week 52; n= 60, 64	-0.12 (± 3.114)	-1.50 (± 2.521)		
Leukocytes; Week 56; n= 59, 61	-0.05 (± 3.357)	-1.50 (± 2.840)		
Leukocytes; Week 60; n= 58, 64	0.19 (± 3.533)	-1.20 (± 2.396)		
Absolute Lymphocytes; Baseline; n= 68, 68	1.638 (± 0.9375)	1.508 (± 0.8230)		
Lymphocytes; Week 4; n= 66, 66	0.031 (± 0.8990)	0.145 (± 0.7485)		
Lymphocytes; Week 8; n= 65, 66	0.245 (± 0.8804)	-0.048 (± 0.6388)		
Lymphocytes; Week 12; n= 63, 65	0.160 (± 0.9043)	-0.071 (± 0.7665)		
Lymphocytes; Week 16; n= 64, 68	0.078 (± 1.0337)	0.079 (± 0.7254)		
Lymphocytes; Week 20; n= 61, 66	0.137 (± 0.7984)	0.127 (± 0.7096)		
Lymphocytes; Week 24; n= 61, 66	0.056 (± 0.8778)	0.011 (± 0.8077)		
Lymphocytes; Week 28; n= 62, 65	0.261 (± 1.0966)	0.004 (± 0.7328)		
Lymphocytes; Week 32; n= 61, 66	0.244 (± 0.9633)	0.031 (± 0.7986)		
Lymphocytes; Week 36; n= 60, 66	0.156 (± 1.0399)	0.031 (± 0.5939)		
Lymphocytes; Week 40; n= 61, 65	0.064 (± 1.0537)	0.037 (± 0.6391)		
Lymphocytes; Week 44; n= 59, 61	0.130 (± 0.8773)	0.059 (± 0.6471)		
Lymphocytes; Week 48; n=59, 64	0.106 (± 0.8396)	0.035 (± 0.7368)		
Lymphocytes; Week 52; n= 60, 64	0.144 (± 0.9262)	0.031 (± 0.6244)		
Lymphocytes; Week 56; n= 59, 61	0.200 (± 0.8356)	0.128 (± 0.7824)		
Lymphocytes; Week 60; n= 58, 64	0.076 (± 0.8821)	-0.101 (± 0.6848)		
Absolute Monocytes; Baseline; n= 68, 68	0.377 (± 0.2126)	0.405 (± 0.2376)		
Monocytes; week 4; n= 66, 66	0.038 (± 0.2444)	0.014 (± 0.2127)		
Monocytes; Week 8; n= 65, 66	0.052 (± 0.2271)	0.039 (± 0.1988)		
Monocytes; Week 12; n= 63, 65	0.077 (± 0.2468)	-0.004 (± 0.1985)		
Monocytes; Week 16; n= 64, 68	0.086 (± 0.2790)	0.031 (± 0.2157)		
Monocytes; Week 20; n= 61, 66	0.132 (± 0.2684)	0.030 (± 0.1967)		
Monocytes; Week 24; n= 61, 66	0.061 (± 0.2290)	0.013 (± 0.2412)		
Monocytes; Week 28; n= 62, 65	0.107 (± 0.2363)	0.035 (± 0.2350)		
Monocytes; Week 32; n= 61, 66	0.108 (± 0.2839)	0.057 (± 0.2069)		

Monocytes; Week 36; n= 60, 66	0.089 (± 0.2992)	0.072 (± 0.2416)		
Monocytes; Week 40; n= 61, 65	0.084 (± 0.2495)	0.050 (± 0.2096)		
Monocytes; Week 44; n= 59, 61	0.090 (± 0.2494)	0.077 (± 0.2176)		
Monocytes; Week 48; n= 59, 64	0.078 (± 0.2261)	0.025 (± 0.2235)		
Monocytes; Week 52; n= 60, 64	0.075 (± 0.2407)	0.024 (± 0.2098)		
Monocytes; Week 56; n= 59, 61	0.051 (± 0.2104)	0.037 (± 0.2303)		
Monocytes; Week 60; n= 58, 64	0.052 (± 0.2600)	0.001 (± 0.2165)		
Absolute Neutrophils; Baseline; n= 68, 68	7.500 (± 2.7424)	7.198 (± 2.9732)		
Neutrophils; Week 4; n= 66, 66	-0.124 (± 2.6170)	-0.583 (± 2.2703)		
Neutrophils; Week 8; n= 65, 66	-0.572 (± 2.6791)	-0.443 (± 2.56476)		
Neutrophils; Week 12; n= 63, 65	-0.797 (± 2.2948)	-0.799 (± 2.6278)		
Neutrophils; Week 16; n= 64, 68	-0.222 (± 2.7666)	-0.914 (± 2.6034)		
Neutrophils; Week 20; n= 61, 66	-0.560 (± 2.3679)	-1.243 (± 2.6857)		
Neutrophils; Week 24; n= 61, 66	-0.980 (± 2.3151)	-1.120 (± 2.8349)		
Neutrophils; Week 28; n= 62, 65	-0.555 (± 2.3719)	-1.335 (± 2.9428)		
Neutrophils; Week 32; n= 61, 66	-0.762 (± 2.4952)	-1.286 (± 2.6995)		
Neutrophils; Week 36; n= 60, 66	-0.509 (± 2.8231)	-1.131 (± 2.4261)		
Neutrophils; Week 40; n= 61, 65	-0.009 (± 3.0467)	-1.010 (± 3.3999)		
Neutrophils; Week 44; n= 59, 61	-0.020 (± 3.3497)	-1.344 (± 2.1031)		
Neutrophils; Week 48; n= 59, 64	-0.403 (± 3.2656)	-1.151 (± 2.5806)		
Neutrophils; Week 52; n= 60, 64	-0.391 (± 3.4463)	-1.211 (± 2.2815)		
Neutrophils; Week 56; n= 59, 61	-0.381 (± 3.4297)	-1.311 (± 3.0024)		
Neutrophils; Week 60; n= 58, 64	-0.048 (± 3.5724)	-0.795 (± 2.6501)		
Absolute Platelets; Baseline; n= 68, 68	259.8 (± 61.16)	270.3 (± 60.86)		
Platelets; Week 4; n= 66, 67	4.5 (± 38.14)	-1.4 (± 33.79)		
Platelets; Week 8; n= 66, 66	5.0 (± 43.97)	4.1 (± 26.48)		
Platelets; Week 12; n= 63, 65	3.1 (± 50.60)	-4.3 (± 37.89)		
Platelets; Week 16; n= 64, 68	15.4 (± 71.20)	1.8 (± 40.25)		
Platelets; Week 20; n= 61, 68	12.3 (± 49.92)	6.1 (± 52.76)		
Platelets; Week 24; n= 62, 65	10.9 (± 50.38)	-4.2 (± 40.07)		
Platelets; Week 28; n= 62, 66	13.3 (± 55.12)	5.4 (± 41.57)		
Platelets; Week 32; n= 61, 67	12.1 (± 45.36)	0.7 (± 43.85)		
Platelets; Week 36; n= 60, 66	9.3 (± 42.64)	0.6 (± 37.87)		
Platelets; Week 40; n= 61, 65	14.7 (± 45.63)	2.0 (± 42.12)		
Platelets; Week 44; n= 60, 63	19.3 (± 48.88)	4.9 (± 40.27)		
Platelets; Week 48; n= 59, 64	14.2 (± 53.93)	5.4 (± 44.80)		

Platelets; Week 52; n= 60, 64	14.7 (± 48.19)	-3.7 (± 46.34)		
Platelets; Week 56; n= 59, 61	20.3 (± 47.35)	-1.0 (± 48.51)		
Platelets; Week 60; n= 59, 64	13.0 (± 50.07)	-2.0 (± 41.32)		

Notes:

[36] - Safety Population

[37] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters of Mean Corpuscle Hemoglobin Concentration (MCHC) and hemoglobin levels

End point title	Change from Baseline in hematology parameters of Mean Corpuscle Hemoglobin Concentration (MCHC) and hemoglobin levels

End point description:

Blood samples were collected to evaluate change from Baseline in MCHC and hemoglobin values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[38]	68[39]		
Units: g/L				
arithmetic mean (standard deviation)				
Absolute MCHC; Baseline; n= 68, 68	324.9 (± 7.53)	324.4 (± 7.37)		
MCHC; Week 4; n= 66, 67	-1.2 (± 6.02)	-1.1 (± 5.92)		
MCHC; Week 8; n= 66, 66	-1.5 (± 6.69)	-1.5 (± 6.86)		
MCHC; Week 12; n= 63, 65	-1.3 (± 7.73)	0.3 (± 6.60)		
MCHC; Week 16; n= 64, 68	-2.3 (± 7.11)	-2.1 (± 7.88)		
MCHC; Week 20; n= 61, 68	-2.2 (± 6.65)	-1.2 (± 7.88)		
MCHC; Week 24; n= 62, 66	-3.2 (± 10.19)	-2.6 (± 7.39)		
MCHC; Week 28; n= 62, 66	-4.3 (± 7.07)	-2.6 (± 7.33)		
MCHC; Week 32; n= 61, 67	-6.6 (± 8.19)	-3.6 (± 7.56)		
MCHC; Week 36; n= 60, 66	-4.7 (± 8.05)	-3.3 (± 8.37)		
MCHC; Week 40; n= 61, 65	-4.5 (± 8.04)	-3.2 (± 8.96)		
MCHC; Week 44; n= 60, 64	-4.7 (± 8.51)	-4.5 (± 9.40)		
MCHC; Week 48; n= 59, 64	-6.0 (± 8.03)	-4.8 (± 10.56)		
MCHC; Week 52; n= 60, 64	-5.2 (± 7.79)	-5.3 (± 7.72)		
MCHC; Week 56; n= 59, 61	-6.9 (± 7.74)	-5.3 (± 7.47)		
MCHC; Week 60; n= 59, 64	-7.5 (± 7.41)	-4.7 (± 9.90)		
Absolute Hemoglobin; Baseline; n= 68, 68	141.6 (± 12.67)	140.6 (± 12.99)		
Hemoglobin; Week 4; n= 66, 67	-2.3 (± 6.86)	-1.8 (± 6.43)		
Hemoglobin; Week 8; n= 66, 66	-2.5 (± 7.56)	-1.1 (± 6.28)		

Hemoglobin; Week 12; n= 63, 65	-1.6 (± 8.28)	-2.2 (± 7.17)		
Hemoglobin; Week 16; n= 64, 68	-1.6 (± 8.24)	-1.9 (± 7.64)		
Hemoglobin; Week 20; n= 61, 68	-0.3 (± 6.85)	-1.4 (± 7.64)		
Hemoglobin; Week 24; n= 62, 66	-1.1 (± 8.06)	-1.6 (± 8.51)		
Hemoglobin; Week 28; n= 62, 66	-1.3 (± 7.48)	-1.3 (± 8.94)		
Hemoglobin; Week 32; n= 61, 67	-1.3 (± 8.03)	-1.6 (± 9.22)		
Hemoglobin; Week 36; n= 60, 66	-0.2 (± 8.50)	-0.4 (± 10.23)		
Hemoglobin; Week 40; n= 61, 65	0.1 (± 8.35)	-0.9 (± 9.74)		
Hemoglobin; Week 44; n= 60, 64	0.7 (± 9.59)	-1.9 (± 10.47)		
Hemoglobin; Week 48; n= 59, 64	0.5 (± 8.20)	-1.9 (± 11.07)		
Hemoglobin; Week 52; n= 60, 64	0.1 (± 8.57)	-1.9 (± 10.36)		
Hemoglobin; Week 56; n= 59, 61	-1.5 (± 9.92)	-1.9 (± 11.48)		
Hemoglobin; Week 60; n= 59, 64	-1.8 (± 9.86)	-2.4 (± 11.36)		

Notes:

[38] - Safety Population

[39] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters of Mean Corpuscle Volume (MCV) levels

End point title	Change from Baseline in hematology parameters of Mean Corpuscle Volume (MCV) levels

End point description:

Blood samples were collected to evaluate change from Baseline in MCV values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[40]	68[41]		
Units: femtoliter (fL)				
arithmetic mean (standard deviation)				
Absolute, Baseline; n= 68, 68	94.8 (± 9.02)	94.8 (± 6.14)		
Week 4; n= 66, 67	0.4 (± 1.67)	0.0 (± 2.33)		
Week 8; n= 66, 66	0.3 (± 2.50)	0.0 (± 2.58)		
Week 12; n= 63, 65	0.2 (± 2.00)	-0.7 (± 2.30)		
Week 16; n= 64, 68	0.0 (± 2.22)	-0.4 (± 2.94)		
Week 20; n= 61, 68	-0.3 (± 1.87)	-0.9 (± 2.66)		
Week 24; n= 62, 66	-0.5 (± 2.21)	-1.0 (± 2.92)		
Week 28; n= 62, 66	-0.4 (± 2.86)	-1.4 (± 3.48)		
Week 32; n= 61, 67	-0.2 (± 3.01)	-1.7 (± 3.56)		
Week 36; n= 60, 66	-0.5 (± 3.55)	-1.9 (± 3.74)		

Week 40; n= 61, 65	-0.9 (± 4.09)	-1.4 (± 3.73)		
Week 44; n= 60, 64	-1.2 (± 5.06)	-1.5 (± 3.91)		
Week 48; n= 59, 64	-1.1 (± 5.96)	-1.5 (± 4.04)		
Week 52; n= 60, 64	-0.8 (± 6.52)	-1.3 (± 4.29)		
Week 56; n= 59, 61	-0.5 (± 6.47)	-1.0 (± 4.15)		
Week 60; n= 59, 64	-0.6 (± 6.57)	-1.0 (± 4.49)		

Notes:

[40] - Safety Population

[41] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters of Mean Corpuscle Hemoglobin (MCH) levels

End point title	Change from Baseline in hematology parameters of Mean Corpuscle Hemoglobin (MCH) levels

End point description:

Blood samples were collected to evaluate change from Baseline in MCH values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[42]	68[43]		
Units: Picogram (pg)				
arithmetic mean (standard deviation)				
Absolute, Baseline; n= 68, 68	30.77 (± 2.902)	30.77 (± 2.255)		
Week 4; n= 66, 67	0.04 (± 0.331)	-0.12 (± 0.785)		
Week 8; n= 66, 66	-0.02 (± 0.950)	-0.16 (± 0.653)		
Week 12; n= 63, 65	-0.04 (± 0.550)	-0.17 (± 0.769)		
Week 16; n= 64, 68	-0.21 (± 0.845)	-0.34 (± 0.769)		
Week 20; n= 61, 68	-0.28 (± 0.665)	-0.41 (± 0.851)		
Week 24; n= 62, 66	-0.45 (± 1.270)	-0.59 (± 0.959)		
Week 28; n= 62, 66	-0.51 (± 0.618)	-0.70 (± 1.184)		
Week 32; n= 61, 67	-0.66 (± 0.764)	-0.88 (± 1.368)		
Week 36; n= 60, 66	-0.60 (± 0.910)	-0.90 (± 1.395)		

Week 40; n= 61, 65	-0.67 (± 1.171)	-0.79 (± 1.390)		
Week 44; n= 60, 64	-0.78 (± 1.566)	-0.95 (± 1.484)		
Week 48; n= 59, 64	-0.87 (± 1.745)	-0.96 (± 1.654)		
Week 52; n= 60, 64	-0.69 (± 1.908)	-0.95 (± 1.585)		
Week 56; n= 59, 61	-0.79 (± 2.056)	-0.83 (± 1.713)		
Week 60; n= 59, 64	-0.86 (± 2.094)	-0.80 (± 1.818)		

Notes:

[42] - Safety Population

[43] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters of erythrocytes levels

End point title	Change from Baseline in hematology parameters of erythrocytes levels

End point description:

Blood samples were collected to evaluate change from Baseline in erythrocytes values at Baseline throughout the 52 weeks study treatment and 8-weeks follow up period. Baseline values were taken at Visit 2 and change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[44]	68[45]		
Units: 10^12 cells/L				
arithmetic mean (standard deviation)				
Absolute, Baseline; n= 68, 68	4.64 (± 0.511)	4.58 (± 0.456)		
Week 4; n= 66, 67	-0.07 (± 0.228)	-0.03 (± 0.226)		
Week 8; n= 66, 66	-0.07 (± 0.278)	-0.01 (± 0.211)		
Week 12; n= 63, 65	-0.04 (± 0.273)	-0.04 (± 0.252)		
Week 16; n= 64, 68	-0.02 (± 0.266)	-0.01 (± 0.243)		
Week 20; n= 61, 68	0.03 (± 0.243)	0.03 (± 0.252)		
Week 24; n= 62, 66	0.02 (± 0.252)	0.05 (± 0.265)		
Week 28; n= 62, 66	0.03 (± 0.286)	0.08 (± 0.264)		
Week 32; n= 61, 67	0.06 (± 0.300)	0.09 (± 0.273)		
Week 36; n= 60, 66	0.08 (± 0.314)	0.14 (± 0.299)		
Week 40; n= 61, 65	0.09 (± 0.274)	0.09 (± 0.270)		

Week 44; n= 60, 64	0.13 (± 0.332)	0.08 (± 0.260)		
Week 48; n= 59, 64	0.14 (± 0.293)	0.10 (± 0.271)		
Week 52; n= 60, 64	0.10 (± 0.309)	0.09 (± 0.251)		
Week 56; n= 59, 61	0.06 (± 0.365)	0.07 (± 0.284)		
Week 60; n= 59, 64	0.07 (± 0.384)	0.05 (± 0.318)		

Notes:

[44] - Safety Population

[45] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-Mepolizumab antibodies

End point title	Number of participants with anti-Mepolizumab antibodies

End point description:

Blood samples were collected for the determination of anti-Mepolizumab antibodies. Participants who showed presence of anti-Mepolizumab antibody were termed as 'positive' and those who did not have anti-Mepolizumab antibody in blood sample were termed as 'negative'. Participants who did not have a positive ADA assay prior to the first dose of investigational product were included in the analysis.

End point type	Secondary

End point timeframe:

Up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[46]	66[47]		
Units: Participants				
Negative	66	65		
Positive	1	1		

Notes:

[46] - Safety Population

[47] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels

End point description:

SBP and DBP were measured from Baseline throughout follow-up (till Week 60) before injection with the participant sitting, having rested in this position for at least 5 minutes before reading. The Baseline value was taken at Visit 2 and change from Baseline was defined as post dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[48]	68[49]		
Units: millimeter of mercury (mm of Hg)				
arithmetic mean (standard deviation)				
Absolute SBP; Baseline; n= 68, 68	127.46 (± 17.794)	122.46 (± 14.134)		
SBP; Week 4; n= 68, 68	0.47 (± 15.865)	0.93 (± 12.370)		
SBP; Week 8; n= 67, 68	0.07 (± 14.192)	1.29 (± 11.066)		
SBP; Week 12; n= 66, 68	-1.12 (± 14.380)	-1.41 (± 12.071)		
SBP; Week 16; n= 64, 68	-0.97 (± 16.630)	-0.41 (± 11.579)		
SBP; Week 20; n= 63, 68	-0.97 (± 15.028)	-0.85 (± 12.019)		
SBP; Week 24; n= 63, 67	-1.54 (± 15.449)	-1.57 (± 12.824)		
SBP; Week 28; n= 63, 67	-0.06 (± 14.337)	-0.15 (± 13.240)		
SBP; Week 32; n= 62, 67	-2.35 (± 14.027)	0.04 (± 11.181)		
SBP; Week 36; n= 62, 67	1.02 (± 14.663)	0.48 (± 14.397)		
SBP; Week 40; n= 62, 66	0.90 (± 14.202)	1.27 (± 12.075)		
SBP; Week 44; n= 61, 66	1.41 (± 16.143)	-0.36 (± 13.694)		
SBP; Week 48; n= 61, 65	-0.41 (± 17.140)	-0.22 (± 12.351)		
SBP: Week 52; n= 61, 65	-1.03 (± 13.200)	-0.32 (± 13.091)		
SBP; Week 56; n= 62, 63	0.06 (± 15.216)	1.02 (± 13.559)		
SBP; Week 60; n= 61, 65	0.61 (± 15.627)	-0.63 (± 11.656)		
Absolute DBP; Baseline; n= 68, 68	80.21 (± 10.127)	76.22 (± 9.646)		
DBP; Week 4; n= 68, 68	-2.26 (± 10.046)	1.01 (± 10.130)		
DBP; Week 8; n= 67, 68	-2.04 (± 8.461)	-0.34 (± 10.078)		
DBP; Week 12; n= 66, 68	-1.92 (± 10.115)	-0.37 (± 9.167)		
DBP; Week 16; n= 64, 68	-1.36 (± 10.237)	0.46 (± 9.824)		
DBP; Week 20; n= 63, 68	-1.25 (± 8.092)	-1.19 (± 9.214)		
DBP; Week 24; n= 63, 67	-2.24 (± 8.751)	-1.16 (± 9.629)		
DBP; Week 28; n= 63, 67	-2.02 (± 9.939)	0.36 (± 10.071)		
DBP; Week 32; n= 62, 67	-4.27 (± 9.313)	-0.49 (± 10.652)		

DBP; Week 36; n= 62, 67	-1.97 (± 10.995)	0.16 (± 10.988)		
DBP; Week 40; n= 62, 66	-0.48 (± 9.625)	-0.03 (± 8.868)		
DBP; Week 44; n= 61, 66	-0.79 (± 9.930)	-1.03 (± 9.595)		
DBP; Week 48; n= 61, 65	-3.26 (± 10.466)	-1.71 (± 9.239)		
DBP; Week 52; n= 61, 65	-3.66 (± 10.628)	-0.06 (± 9.236)		
DBP; Week 56; n= 62, 63	-3.48 (± 10.570)	0.11 (± 8.899)		
DBP; Week 60; n= 61, 65	-2.54 (± 11.278)	-0.45 (± 9.836)		

Notes:

[48] - Safety Population

[49] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse rate

End point title	Change from Baseline in pulse rate

End point description:

Pulse rate was measured from Baseline throughout follow-up (till Week 60) before injection with the participant sitting, having rested in this position for at least 5 minutes before reading. The Baseline value was taken at Visit 2 and change from Baseline was defined as post dose visit value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[50]	68[51]		
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)				
Absolute Baseline; n= 68, 68	77.38 (± 13.763)	75.75 (± 10.404)		
Week 4; n= 68, 68	2.01 (± 12.294)	1.87 (± 10.543)		
Week 8; n= 67, 68	0.97 (± 10.718)	-1.01 (± 10.304)		
Week 12; n= 66, 68	1.52 (± 12.393)	-0.12 (± 10.855)		
Week 16; n= 64, 68	0.59 (± 11.287)	0.44 (± 11.411)		
Week 20; n= 63, 68	1.03 (± 11.521)	-0.56 (± 9.687)		
Week 24; n= 63, 67	0.79 (± 12.134)	0.37 (± 10.057)		

Week 28; n= 62, 67	1.29 (± 10.439)	0.16 (± 10.093)		
Week 32; n= 62, 67	1.60 (± 11.703)	-0.31 (± 10.530)		
Week 36; n= 62, 67	3.47 (± 12.538)	-0.57 (± 11.422)		
Week 40; n= 62, 66	2.65 (± 12.297)	0.74 (± 11.669)		
Week 44; n= 61, 66	3.10 (± 12.195)	0.15 (± 12.763)		
Week 48; n= 61, 65	3.85 (± 12.383)	-1.12 (± 10.315)		
Week 52; n= 61, 65	1.85 (± 11.987)	-2.17 (± 9.596)		
Week 56; n= 62, 63	2.60 (± 14.041)	-0.35 (± 9.986)		
Week 60; n= 61, 65	1.51 (± 12.793)	0.09 (± 10.280)		

Notes:

[50] - Safety Population

[51] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in body temperature

End point title	Change from Baseline in body temperature

End point description:

Body temperature was measured from Baseline throughout follow-up (till Week 60). The Baseline value was taken at Visit 2 and change from Baseline was defined as post dose visit value minus Baseline value. The analysis was performed on Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Mean and standard deviation (SD) were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[52]	68[53]		
Units: Degree celsius				
arithmetic mean (standard deviation)				
Absolute Baseline; n= 68, 68	36.52 (± 0.385)	36.51 (± 0.462)		
Week 4; n= 68, 68	0.05 (± 0.439)	-0.04 (± 0.411)		
Week 8; n= 67,68	-0.01 (± 0.379)	-0.02 (± 0.425)		
Week 12; n= 66, 68	0.05 (± 0.410)	-0.03 (± 0.447)		
Week 16; n= 64, 68	-0.01 (± 0.421)	-0.03 (± 0.432)		

Week 20; n= 63, 68	-0.08 (± 0.351)	-0.13 (± 0.376)		
Week 24; n= 62, 67	-0.06 (± 0.449)	-0.06 (± 0.389)		
Week 28; n= 63, 67	-0.06 (± 0.499)	-0.14 (± 0.411)		
Week 32; n= 62, 67	-0.09 (± 0.392)	-0.07 (± 0.355)		
Week 36; n= 62, 67	-0.05 (± 0.431)	0.03 (± 0.468)		
Week 40; n= 62, 66	-0.03 (± 0.530)	-0.13 (± 0.406)		
Week 44; n= 61, 65	-0.03 (± 0.550)	-0.08 (± 0.396)		
Week 48; n= 61, 64	-0.04 (± 0.452)	-0.09 (± 0.414)		
Week 52; n= 60, 65	-0.04 (± 0.423)	-0.12 (± 0.541)		
Week 56; n= 61, 63	-0.08 (± 0.530)	0.00 (± 0.402)		
Week 60; n= 61, 64	0.03 (± 0.467)	-0.02 (± 0.479)		

Notes:

[52] - Safety Population

[53] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in QT interval corrected by Fridericia's method (QTcF) and QT interval corrected by Bazett's method (QTcB) values

End point title	Mean change from Baseline in QT interval corrected by Fridericia's method (QTcF) and QT interval corrected by Bazett's method (QTcB) values

End point description:

Single measurements of 12-lead electrocardiogram (ECGs) were obtained after 5 minutes rest in a supine position at Baseline throughout the 52 weeks treatment period and 8 weeks follow-up period using an ECG machine. Mean change from Baseline in QTcF and QTcB values were measured. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[54]	68[55]		
Units: milliseconds (msec)				
arithmetic mean (standard deviation)				
QTcF; Week 8; n= 66, 66	0.1 (± 17.90)	1.0 (± 15.03)		
QTcF; Week 16; n= 64, 66	0.8 (± 15.26)	0.2 (± 14.05)		
QTcF; Week 24; n= 60, 66	2.8 (± 14.43)	1.9 (± 16.66)		
QTcF; Week 32; n= 61, 66	6.2 (± 25.19)	1.5 (± 17.16)		

QTcF; Week 40; n= 61, 65	-0.5 (± 15.25)	-0.3 (± 17.53)		
QTcF; Week 52; n= 58, 64	2.0 (± 15.96)	3.0 (± 16.04)		
QTcF; Week 60; n= 58, 63	3.0 (± 14.30)	2.9 (± 14.97)		
QTcF; Any time post Baseline; n= 68, 68	16.9 (± 23.74)	15.4 (± 13.79)		
QTcB; Week 8; n= 66, 66	-0.8 (± 19.05)	0.9 (± 17.31)		
QTcB; Week 16; n= 64, 66	-0.1 (± 18.33)	-0.9 (± 14.76)		
QTcB; Week 24; n= 60, 66	1.4 (± 17.89)	1.0 (± 18.10)		
QTcB; Week 32; n= 61, 66	5.2 (± 29.63)	0.0 (± 19.63)		
QTcB; Week 40; n= 61, 65	-0.6 (± 17.83)	-1.4 (± 18.88)		
QTcB; Week 52; n= 58, 64	1.8 (± 17.64)	0.7 (± 18.27)		
QTcB; Week 60; n= 58, 63	1.2 (± 16.56)	2.7 (± 17.27)		
QTcB; Any time post Baseline; n= 68, 68	18.8 (± 26.46)	18.1 (± 15.28)		

Notes:

[54] - Safety Population

[55] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum change from Baseline in QTcF and QTcB values

End point title	Maximum change from Baseline in QTcF and QTcB values

End point description:

Single measurements of 12-lead ECGs were obtained after 5 minutes rest in a supine position at Baseline throughout the 52 weeks treatment period and 8 weeks follow-up period using an ECG machine. Maximum change from Baseline in QTcF and QTcB values were measured.

End point type	Secondary

End point timeframe:

Baseline and up to Week 60

End point values	Placebo	Mepolizumab 300mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[56]	68[57]		
Units: msec				
arithmetic mean (standard deviation)				
QTcB interval	18.8 (± 26.46)	18.1 (± 15.28)		
QTcF interval	16.9 (± 23.74)	15.4 (± 13.79)		

Notes:

[56] - Safety Population

[57] - Safety Population

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 start of the study treatment until week 52.

Adverse event reporting additional description:

AEs and SAEs were collected in Safety Population which comprised of all participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Mepolizumab 300mg

Reporting group description:

Participants received Mepolizumab 300mg injection via SC route once every 4 weeks along with SOC drugs up to Week 48.

Reporting group title	Placebo

Reporting group description:

Participants received placebo injection via subcutaneous (SC) route once every 4 weeks along with standard of care (SOC) drugs up to Week 48.

Serious adverse events	Mepolizumab 300mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 68 (17.65%)	18 / 68 (26.47%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testis cancer			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			

subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebellar ischaemia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			

subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nystagmus			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pachymeningitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic granulomatous angiitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 68 (2.94%)	4 / 68 (5.88%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 68 (0.00%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 68 (0.00%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 68 (0.00%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterococcal infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory infection			
subjects affected / exposed	0 / 68 (0.00%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Mepolizumab 300mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 68 (95.59%)	61 / 68 (89.71%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 68 (14.71%)	10 / 68 (14.71%)	
occurrences (all)	13	14	
Injection site reaction			
subjects affected / exposed	9 / 68 (13.24%)	7 / 68 (10.29%)	
occurrences (all)	38	11	
Pyrexia			
subjects affected / exposed	7 / 68 (10.29%)	7 / 68 (10.29%)	
occurrences (all)	12	12	
Asthenia			
subjects affected / exposed	5 / 68 (7.35%)	3 / 68 (4.41%)	
occurrences (all)	43	18	
Chest pain			
subjects affected / exposed	1 / 68 (1.47%)	5 / 68 (7.35%)	
occurrences (all)	3	5	
Injection site pain			
subjects affected / exposed	2 / 68 (2.94%)	3 / 68 (4.41%)	
occurrences (all)	3	15	
Oedema peripheral			
subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	4	1	
Influenza like illness			

subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	10 / 68 (14.71%)	7 / 68 (10.29%)	
occurrences (all)	14	11	
Cough			
subjects affected / exposed	5 / 68 (7.35%)	8 / 68 (11.76%)	
occurrences (all)	5	12	
Oropharyngeal pain			
subjects affected / exposed	8 / 68 (11.76%)	5 / 68 (7.35%)	
occurrences (all)	8	5	
Productive cough			
subjects affected / exposed	6 / 68 (8.82%)	7 / 68 (10.29%)	
occurrences (all)	8	15	
Sinus congestion			
subjects affected / exposed	6 / 68 (8.82%)	6 / 68 (8.82%)	
occurrences (all)	9	9	
Wheezing			
subjects affected / exposed	5 / 68 (7.35%)	6 / 68 (8.82%)	
occurrences (all)	9	7	
Nasal congestion			
subjects affected / exposed	4 / 68 (5.88%)	5 / 68 (7.35%)	
occurrences (all)	4	6	
Upper-airway cough syndrome			
subjects affected / exposed	2 / 68 (2.94%)	6 / 68 (8.82%)	
occurrences (all)	2	6	
Dyspnoea			
subjects affected / exposed	1 / 68 (1.47%)	4 / 68 (5.88%)	
occurrences (all)	1	4	
Epistaxis			
subjects affected / exposed	3 / 68 (4.41%)	2 / 68 (2.94%)	
occurrences (all)	3	8	
Sneezing			

subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	3	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 68 (2.94%)	4 / 68 (5.88%)	
occurrences (all)	3	5	
Investigations			
Weight increased			
subjects affected / exposed	4 / 68 (5.88%)	1 / 68 (1.47%)	
occurrences (all)	5	1	
Alanine aminotransferase increased			
subjects affected / exposed	5 / 68 (7.35%)	0 / 68 (0.00%)	
occurrences (all)	5	0	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	3	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	3 / 68 (4.41%)	2 / 68 (2.94%)	
occurrences (all)	3	4	
Ligament sprain			
subjects affected / exposed	4 / 68 (5.88%)	1 / 68 (1.47%)	
occurrences (all)	4	1	
Contusion			
subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	3	1	
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 68 (32.35%)	12 / 68 (17.65%)	
occurrences (all)	50	20	
Dizziness			

subjects affected / exposed	3 / 68 (4.41%)	5 / 68 (7.35%)	
occurrences (all)	6	8	
Paraesthesia			
subjects affected / exposed	4 / 68 (5.88%)	3 / 68 (4.41%)	
occurrences (all)	4	4	
Sinus headache			
subjects affected / exposed	2 / 68 (2.94%)	3 / 68 (4.41%)	
occurrences (all)	4	4	
Migraine			
subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	3	1	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 68 (1.47%)	4 / 68 (5.88%)	
occurrences (all)	1	5	
Vertigo			
subjects affected / exposed	5 / 68 (7.35%)	1 / 68 (1.47%)	
occurrences (all)	5	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	4 / 68 (5.88%)	2 / 68 (2.94%)	
occurrences (all)	4	2	
Cataract			
subjects affected / exposed	3 / 68 (4.41%)	2 / 68 (2.94%)	
occurrences (all)	3	2	
Eye pruritus			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 68 (16.18%)	13 / 68 (19.12%)	
occurrences (all)	16	14	
Diarrhoea			
subjects affected / exposed	12 / 68 (17.65%)	8 / 68 (11.76%)	
occurrences (all)	16	9	
Vomiting			

subjects affected / exposed	11 / 68 (16.18%)	4 / 68 (5.88%)	
occurrences (all)	12	4	
Abdominal pain upper			
subjects affected / exposed	5 / 68 (7.35%)	5 / 68 (7.35%)	
occurrences (all)	11	5	
Abdominal pain			
subjects affected / exposed	2 / 68 (2.94%)	4 / 68 (5.88%)	
occurrences (all)	2	4	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 68 (1.47%)	4 / 68 (5.88%)	
occurrences (all)	1	5	
Dyspepsia			
subjects affected / exposed	1 / 68 (1.47%)	3 / 68 (4.41%)	
occurrences (all)	3	3	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 68 (13.24%)	6 / 68 (8.82%)	
occurrences (all)	10	7	
Pruritus			
subjects affected / exposed	6 / 68 (8.82%)	1 / 68 (1.47%)	
occurrences (all)	7	1	
Urticaria			
subjects affected / exposed	4 / 68 (5.88%)	1 / 68 (1.47%)	
occurrences (all)	7	1	
Skin lesion			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	4	0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	3 / 68 (4.41%)	0 / 68 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 68 (22.06%)	12 / 68 (17.65%)	
occurrences (all)	17	22	
Myalgia			

subjects affected / exposed	6 / 68 (8.82%)	9 / 68 (13.24%)	
occurrences (all)	8	12	
Back pain			
subjects affected / exposed	8 / 68 (11.76%)	6 / 68 (8.82%)	
occurrences (all)	10	10	
Pain in extremity			
subjects affected / exposed	5 / 68 (7.35%)	6 / 68 (8.82%)	
occurrences (all)	5	7	
Neck pain			
subjects affected / exposed	8 / 68 (11.76%)	2 / 68 (2.94%)	
occurrences (all)	9	2	
Musculoskeletal pain			
subjects affected / exposed	6 / 68 (8.82%)	2 / 68 (2.94%)	
occurrences (all)	7	2	
Joint swelling			
subjects affected / exposed	2 / 68 (2.94%)	3 / 68 (4.41%)	
occurrences (all)	2	3	
Muscle spasms			
subjects affected / exposed	3 / 68 (4.41%)	2 / 68 (2.94%)	
occurrences (all)	3	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 68 (17.65%)	16 / 68 (23.53%)	
occurrences (all)	19	25	
Sinusitis			
subjects affected / exposed	14 / 68 (20.59%)	11 / 68 (16.18%)	
occurrences (all)	15	19	
Upper respiratory tract infection			
subjects affected / exposed	14 / 68 (20.59%)	11 / 68 (16.18%)	
occurrences (all)	21	14	
Bronchitis			
subjects affected / exposed	7 / 68 (10.29%)	8 / 68 (11.76%)	
occurrences (all)	9	9	
Influenza			
subjects affected / exposed	7 / 68 (10.29%)	6 / 68 (8.82%)	
occurrences (all)	9	6	

Urinary tract infection			
subjects affected / exposed	5 / 68 (7.35%)	4 / 68 (5.88%)	
occurrences (all)	5	6	
Respiratory tract infection			
subjects affected / exposed	5 / 68 (7.35%)	8 / 68 (11.76%)	
occurrences (all)	7	15	
Acute sinusitis			
subjects affected / exposed	6 / 68 (8.82%)	2 / 68 (2.94%)	
occurrences (all)	6	3	
Conjunctivitis			
subjects affected / exposed	4 / 68 (5.88%)	4 / 68 (5.88%)	
occurrences (all)	4	4	
Rhinitis			
subjects affected / exposed	5 / 68 (7.35%)	3 / 68 (4.41%)	
occurrences (all)	5	3	
Ear infection			
subjects affected / exposed	1 / 68 (1.47%)	6 / 68 (8.82%)	
occurrences (all)	1	8	
Fungal skin infection			
subjects affected / exposed	4 / 68 (5.88%)	3 / 68 (4.41%)	
occurrences (all)	4	3	
Oral herpes			
subjects affected / exposed	4 / 68 (5.88%)	3 / 68 (4.41%)	
occurrences (all)	6	5	
Gastroenteritis			
subjects affected / exposed	5 / 68 (7.35%)	1 / 68 (1.47%)	
occurrences (all)	5	1	
Otitis media			
subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	3	1	
Viral infection			
subjects affected / exposed	3 / 68 (4.41%)	1 / 68 (1.47%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2013	Generated to remove evaluation of ACQ-6 and sino-nasal symptoms at the time of relapse and to clarify the definition of time of onset of relapse; countryspecific requirements for Japan regarding hepatitis B screening added as well as clarification to text as needed and administrative changes
27 August 2014	Generated to clarify investigators can taper oral corticosteroids downward when BVAS≠0; to include additional statement in risk assessment table; to clarify that participants who become pregnant must be withdrawn from study treatment; to clarify requirements for collection of a fasting blood sample in diabetic participants; to clarify that collection of PK samples at Weeks 1 and 29 is optional; to delete requirement for measurement of eosinophil count as a liver event follow-up assessment; to amend the schedule for sputum sampling in the biomarker sub-study; to add country-specific change for Japan regarding definition of relapsing disease in inclusion criteria; to include SAMAs and LAMAs as bronchodilator to be withheld prior to reversibility testing; to clarify requirements for participant follow-up in the event study treatment is discontinued; to include reference to the Supplement to Version 12 of the Investigator's Brochure and other administrative changes.
24 June 2016	Generated to add secondary endpoints including the remission definition as per the EULAR recommendations for conducting clinical trials in systemic vasculitis, i.e., BVAS=0 and prednisolone/prednisone dose ≤7.5 mg/day, to clarify relapse definition, to amend the statistical analysis plan in accordance with the addition of the new secondary endpoints, to clarify specific aspects of the Data Analysis and Statistical Considerations section and to include some administrative updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported