# 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 | v1 |
| This version publication date | 14 September 2017 |
| First version publication date | 14 September 2017 |

## 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, Subject, Assessor |

### 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<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br>48.2<br>± 14.32 | <br><br>48.7<br>± 12.39 | <br><br><br>- |
| Gender categorical<br>Units: Subjects | | | |
| Female | 38 | 42 | 80 |
| Male | 30 | 26 | 56 |
| Race/Ethnicity, Customized<br>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: Total accrued number of weeks where remission achieved over the study treatment period

| | |
|---|---|
| End point title | Total accrued number of weeks where remission achieved over the study treatment period |
| 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: Weeks | | | | |
| 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 proportion 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 | | | | |
| Endpoint (event) | 56 | 38 | | |
| Censored | 12 | 30 | | |

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 |
| P-value | < 0.001 [8] |
| Method | Wald Chi-Square |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 0.322 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.206 |
| upper limit | 0.502 |

Notes:

[8] - 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: Average daily prednisolone/prednisone dose during the last 4 weeks of the Study Treatment Period

| End point title | 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[9] | 68[10] | | |
| Units: Milligrams (mg) | | | | |
| number (not applicable) | | | | |
| Zero | 2 | 12 | | |
| >0 to <=4.0mg | 3 | 18 | | |
| >4.0 to <=7.5mg | 18 | 10 | | |
| >7.5mg | 45 | 28 | | |

Notes:

[9] - ITT Population

[10] - 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 [11] |
| 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:

[11] - 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[12] | 68[13] | | |
| Units: Participants | | | | |
| Participants | 1 | 13 | | |

Notes:

[12] - ITT Population

[13] - 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: Total accrued number of weeks where remission achieved over the study treatment period

| End point title | Total accrued number of weeks where remission achieved over the study treatment period |
|---|---|

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[14] | 68[15] | | |
| Units: Weeks | | | | |
| 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:

[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 | < 0.001 [16] |
| 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:

[16] - 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 proportion 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 with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region. Statistical analysis was performed 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[17] | 68[18] | | |
| Units: Participants | | | | |
| Participants | 7 | 28 | | |

Notes:

[17] - ITT Population

[18] - 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 [19] |
| 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:

[19] - 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 proportion of participants who achieved remission (i.e., BVAS=0 and prednisolone/prednisone <=7.5 mg/day) within the first 24 weeks of the study and remain in remission for the reminder of the study treatment period was reported. The statistical analysis was performed using a logistic regression model with covariates including treatment group, Baseline prednisolone/prednisone daily dose, Baseline BVAS score and region. Statistical analysis was performed on ITT Population. The odds ratio for

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[20] | 68[21] | | |
| Units: Participants | | | | |
| Participants | 2 | 16 | | |

Notes:

[20] - ITT Population

[21] - 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[22] | 68[23] | | |
| 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:

[22] - Safety Population

[23] - 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[24] | 68[25] | | |
| 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 (± 12.3) | | |
| 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 (± 11.3) | | |
| ALT; Week 36; n= 60, 67 | -0.1 (± 6.21) | -3 (± 11.66) | | |
| ALT; Week 40; n= 61, 66 | 0.3 (± 9.01) | -2.3 (± 11.7) | | |
| 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 (± 20.9) | | |
| 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 (± 11.24) | 4.4 (± 21.9) | | |
| 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 (± 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 (± 12.3) | 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 (± 15.08) | | |
| Absolute AST; Baseline; n= 68, 68 | 19.3 (± 6.11) | 21.8 (± 10.73) | | |
| AST; Week 4; n= 68, 68 | 0 (± 4.41) | -1.7 (± 8.61) | | |
| AST; Week 8; n= 67, 66 | -0.4 (± 4.77) | -1 (± 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 (± 7.9) | | |
| AST; Week 20; n= 63, 68 | 0.8 (± 4.66) | -0.6 (± 8.49) | | |
| AST; Week 24; n= 63, 66 | 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 (± 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 (± 75.99) | 88.8 (± 75.18) | | |
| Creatinine kinase; Week 4; n= 68, 68 | -2.4 (± 83.23) | 2 (± 60.92) | | |
| Creatinine kinase; Week 8; n= 67, 66 | -5 (± 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 (± 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 (± 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 (± 11.7) | -2 (± 9.68) | | |
| GGT; Week 8; n= 67, 66 | -1 (± 8.59) | -0.6 (± 17.99) | | |
| GGT; Week 12; n= 65, 68 | -2.9 (± 6.68) | -1.9 (± 18.7) | | |
| 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 (± 24.5) | | |
| 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 (± 16.51) | | |
| GGT; Week 52; n= 60, 65 | -1.6 (± 16.44) | -4.2 (± 13.53) | | |
| GGT; Week 56; n= 61, 63 | -5 (± 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 (± 27.8) | | |
| 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 (± 26.8) | -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 (± 33.4) | -17 (± 31.37) | | |
| Lactate dehydro; Week 48; n= 61, 64 | 0.8 (± 43.82) | -19 (± 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 (± 30.87) | | |
| Lactate dehydro; Week 60; n= 60, 65 | -3.5 (± 34.15) | -12.4 (± 33.23) | | |

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 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[26] | 68[27] | | |
| 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 (± 2.8) | 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 (± 3.1) | | |
| 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) | -0.5 (± 3.19) | | |
| Protein; Week 8; n= 67, 66 | -1.5 (± 2.97) | -0.9 (± 3.6) | | |
| Protein; Week 12; n= 65, 68 | -0.6 (± 3.57) | -0.6 (± 3.3) | | |

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|---|---|---|---|---|
| Protein; Week 16; n= 65, 68 | -0.3 (± 3.56) | -0.8 (± 3.93) | | |
| Protein; Week 20; n= 63, 68 | 0 (± 3.21) | 0.1 (± 4.28) | | |
| Protein; Week 24; n= 63, 66 | 0.2 (± 3.99) | 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:

[26] - Safety Population

[27] - 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[28] | 68[29] | | |
| Units: micromole per liter (µmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Absolute Total bilirubin; Baseline; n= 68, 68 | 9.8 (± 6.14) | 8.8 (± 4.1) | | |
| 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 (± 3.5) | | |
| 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 (± 4.14) | | |
| Total bilirubin; Week 20; n= 63, 68 | -0.5 (± 2.9) | 0.3 (± 3.57) | | |
| Total bilirubin; Week 24; n= 63, 66 | -0.3 (± 3.36) | 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 (± 2.5) | 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 (± 3.42) | | |
| Absolute Creatinine; Baseline; n= 68, 68 | 75.49 (± 12.878) | 73 (± 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 | 1.5 (± 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) | 2.6 (± 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) | 0.4 (± 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 (± 9.07) | | |
| 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) | -0.3 (± 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 (± 1.06) | 0 (± 0.84) | | |
| Direct bilirubin; Week 8; n= 67, 66 | 0 (± 1.01) | 0.1 (± 0.96) | | |
| Direct bilirubin; Week 12; n= 65, 68 | 0 (± 0.97) | 0 (± 1.04) | | |
| Direct bilirubin; Week 16; n= 65, 68 | -0.2 (± 0.96) | -0.1 (± 1.2) | | |
| Direct bilirubin; Week 20; n= 63, 68 | 0 (± 0.86) | 0.1 (± 1.03) | | |
| Direct bilirubin; Week 24; n= 63, 66 | 0.1 (± 0.9) | 0 (± 0.88) | | |
| Direct bilirubin; Week 28; n= 62, 66 | -0.1 (± 1.2) | 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 (± 1.11) | 0 (± 0.94) | | |
| Direct bilirubin; Week 44; n= 61, 66 | 0.1 (± 0.93) | 0 (± 1.12) | | |
| Direct bilirubin; Week 48; n= 61, 64 | 0.1 (± 0.99) | 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 (± 1.1) | 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 (± 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) | | |
| Indirect bilirubin; Week 24; n= 63, 66 | -0.4 (± 2.94) | 0 (± 2.37) | | |
| Indirect bilirubin; Week 28; n= 62, 66 | -0.7 (± 2.6) | 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 (± 3.3) | | |
| 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:

[28] - Safety Population

[29] - 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[30] | 68[31] | | |
| 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 (± 0.12) | | |
| Calcium; Week 8; n= 67, 66 | -0.013 (± 0.0877) | -0.01 (± 0.1003) | | |
| Calcium; Week 12; n= 65, 68 | -0.013 (± 0.0844) | -0.026 (± 0.0889) | | |
| Calcium; Week 16; n= 65, 68 | 0 (± 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 (± 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) | -0.02 (± 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 (± 0.111) | | |
| 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 (± 2.21) | | |
| Chloride; Week 4; n= 68, 68 | 0.6 (± 1.97) | 0.2 (± 2) | | |
| 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 (± 2.2) | | |
| 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 (± 2.2) | | |
| 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 (± 2.2) | | |
| Absolute Cholesterol; Baseline; n= 68, 68 | 5.771 (± 1.2033) | 5.788 (± 1.2386) | | |
| Cholesterol; Week 8; n= 2, 0 | -0.25 (± 0.1414) | 99999 (± 99999) | | |
| Cholesterol; Week 12; n= 1, 0 | 0.05 (± 99999) | 99999 (± 99999) | | |
| Cholesterol; Week 16; n= 1, 1 | -0.4 (± 99999) | -0.3 (± 99999) | | |
| Cholesterol; Week 20; n= 1, 1 | 0.05 (± 99999) | -0.3 (± 99999) | | |
| Cholesterol; Week 24; n= 0, 1 | 99999 (± 99999) | -0.56 (± 99999) | | |
| Cholesterol; Week 36; n= 0, 1 | 99999 (± 99999) | 0.42 (± 99999) | | |
| Cholesterol; Week 52; n= 60, 65 | -0.006 (± 0.9364) | -0.384 (± 0.8798) | | |
| Cholesterol; Week 56; n= 1, 0 | -0.22 (± 99999) | 99999 (± 99999) | | |
| Absolute Glucose; Baseline; n= 68, 68 | 5.76 (± 2) | 5.35 (± 1.195) | | |
| Glucose; Week 4; n= 68, 68 | 0.27 (± 1.619) | -0.01 (± 1.05) | | |
| 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) | | |

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|---|---|---|---|---|
| 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 (± 1.74) | | |
| Glucose; Week 52; n= 60, 65 | -0.17 (± 1.65) | 0.02 (± 1.258) | | |
| Glucose; Week 56; n= 61, 63 | 0.01 (± 1.718) | 0.13 (± 1.852) | | |
| Glucose; Week 60; n= 60, 65 | 0.2 (± 1.664) | 0.11 (± 1.483) | | |
| Absolute HDL cholesterol; Baseline; n= 68, 68 | 1.837 (± 0.454) | 1.937 (± 0.5606) | | |
| HDL cholesterol; Week 8; n= 2, 0 | -0.075 (± 0.0354) | 99999 (± 99999) | | |
| HDL cholesterol; Week 12; n= 1, 0 | -0.1 (± 99999) | 99999 (± 99999) | | |
| HDL cholesterol; Week 16; n= 1, 1 | 0.4 (± 99999) | -0.15 (± 99999) | | |
| HDL cholesterol; Week 20; n= 1, 1 | 0 (± 99999) | -0.25 (± 99999) | | |
| HDL cholesterol; Week 24; n= 0, 1 | 99999 (± 99999) | -0.39 (± 99999) | | |
| HDL cholesterol; Week 36; n= 0, 1 | 99999 (± 99999) | 0.4 (± 99999) | | |
| HDL cholesterol; Week 52; n= 60, 65 | -0.045 (± 0.2832) | -0.15 (± 0.3146) | | |
| HDL cholesterol; Week 56; n= 1, 0 | -0.06 (± 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 | -0.35 (± 99999) | 99999 (± 99999) | | |
| LDL cholesterol; Week 12; n= 1, 0 | 0.19 (± 99999) | 99999 (± 99999) | | |
| LDL cholesterol; Week 16; n= 1, 1 | -0.73 (± 99999) | -0.79 (± 99999) | | |
| LDL cholesterol; Week 20; n= 1, 1 | -0.15 (± 99999) | -0.54 (± 99999) | | |
| LDL cholesterol; Week 24; n= 0, 1 | 99999 (± 99999) | 0.04 (± 99999) | | |
| LDL cholesterol; Week 36; n= 0, 1 | 99999 (± 99999) | 0.25 (± 99999) | | |
| LDL cholesterol; Week 52; n= 58, 64 | 0.016 (± 0.7717) | -0.215 (± 0.8079) | | |
| LDL cholesterol; Week 56; n= 1, 0 | 0.1 (± 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) | | |

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|---|---|---|---|---|
| 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) | 0.04 (± 0.2172) | | |
| Phosphate; Week 36; n= 60, 67 | -0.038 (± 0.2159) | 0.023 (± 0.226) | | |
| 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 (± 0.224) | | |
| Phosphate; Week 48; n= 61, 64 | -0.053 (± 0.1931) | -0.02 (± 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) | 4.1 (± 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 (± 0.34) | 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 (± 0.35) | | |
| Potassium; Week 28; n= 61, 66 | 0.07 (± 0.338) | 0.1 (± 0.382) | | |
| Potassium; Week 32; n= 61, 67 | 0.04 (± 0.34) | 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 (± 0.358) | 0.1 (± 0.39) | | |
| 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 (± 1.46) | -0.1 (± 1.91) | | |
| Sodium; Week 20; n= 63, 68 | 0 (± 1.88) | 0.1 (± 2.09) | | |
| Sodium; Week 24; n= 63, 66 | 0.2 (± 1.94) | 0 (± 1.95) | | |
| Sodium; Week 28; n= 62, 66 | 0.5 (± 1.71) | 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 (± 2.1) | 0 (± 1.95) | | |
| Sodium; Week 40; n= 61, 66 | 0.2 (± 2.42) | 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) | | |

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|---|---|---|---|---|
| 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) | 0.2 (± 1.206) | | |
| Urea; Week 12; n= 65, 68 | -0.15 (± 1.414) | -0.1 (± 1.217) | | |
| Urea; Week 16; n= 65, 68 | -0.07 (± 1.569) | 0 (± 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 (± 1.35) | | |
| Urea; Week 32; n= 61, 67 | -0.11 (± 1.32) | -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) | -0.1 (± 1.17) | | |
| Absolute VLDL cholesterol; Baseline; n= 67, 68 | 0.68 (± 0.2846) | 0.646 (± 0.2841) | | |
| VLDL cholesterol; Week 8; n= 1, 0 | 0.1 (± 99999) | 99999 (± 99999) | | |
| VLDL cholesterol; Week 12; n= 1, 0 | -0.04 (± 99999) | 99999 (± 99999) | | |
| VLDL cholesterol; Week 16; n= 1, 1 | -0.07 (± 99999) | 0.64 (± 99999) | | |
| VLDL cholesterol; Week 20; n= 1, 1 | 0.2 (± 99999) | 0.49 (± 99999) | | |
| VLDL cholesterol; Week 24; n= 0, 1 | 99999 (± 99999) | -0.21 (± 99999) | | |
| VLDL cholesterol; Week 36; n= 0, 1 | 99999 (± 99999) | -0.23 (± 99999) | | |
| VLDL cholesterol; Week 52; n= 58, 64 | -0.019 (± 0.3229) | -0.051 (± 0.1927) | | |
| VLDL cholesterol; Week 56; n= 1, 0 | -0.26 (± 99999) | 99999 (± 99999) | | |

Notes:

[30] - Safety Population

[31] - 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[32] | 68[33] | | |
| Units: µg/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Absolute Troponin; Baseline; n= 68, 68 | 0.013 (± 0.011) | 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 (± 0.009) | | |
| Troponin; Week 32; n= 61, 67 | -0.003 (± 0.01) | -0.002 (± 0.0092) | | |
| Troponin; Week 36; n= 61, 67 | -0.002 (± 0.0107) | 0 (± 0.0185) | | |
| Troponin; Week 40; n= 61, 66 | -0.001 (± 0.0117) | -0.002 (± 0.009) | | |
| Troponin; Week 44; n= 61, 65 | 0 (± 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:

[32] - Safety Population

[33] - 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[34] | 68[35] | | |
| Units: 10^9/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Absolute Basophils; Baselin; n= 68, 68 | 0.03 (± 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 | 0.01 (± 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 (± 0.0296) | | |
| Basophils; Week 48; n= 59, 64 | 0.003 (± 0.0408) | -0.004 (± 0.03) | | |
| 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) | | |

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|---|---|---|---|---|
| Eosinophils; Week 4; n= 66, 66 | -0.054 (± 0.3309) | -0.339 (± 0.6794) | | |
| Eosinophils; Week 8; n= 65, 66 | 0.103 (± 0.2921) | -0.37 (± 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 (± 0.828) | | |
| Eosinophils; Week 20; n= 61, 66 | 0.162 (± 0.59) | -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) | -0.36 (± 0.8258) | | |
| Eosinophils; Week 32; n= 61, 66 | 0.079 (± 0.3759) | -0.347 (± 0.831) | | |
| 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 (± 0.854) | | |
| 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 (± 3.13) | | |
| 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 (± 2.11) | -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 | -0.1 (± 3.092) | -1.46 (± 2.546) | | |
| Leukocytes; Week 52; n= 60, 64 | -0.12 (± 3.114) | -1.5 (± 2.521) | | |
| Leukocytes; Week 56; n= 59, 61 | -0.05 (± 3.357) | -1.5 (± 2.84) | | |
| Leukocytes; Week 60; n= 58, 64 | 0.19 (± 3.533) | -1.2 (± 2.396) | | |

| | | | | |
|---|---|---|---|---|
| Absolute Lymphocytes; Baseline; n= 68, 68 | 1.638 (± 0.9375) | 1.508 (± 0.823) | | |
| Lymphocytes; Week 4; n= 66, 66 | 0.031 (± 0.899) | 0.145 (± 0.7485) | | |
| Lymphocytes; Week 8; n= 65, 66 | 0.245 (± 0.8804) | -0.048 (± 0.6388) | | |
| Lymphocytes; Week 12; n= 63, 65 | 0.16 (± 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 | 0.13 (± 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 | 0.2 (± 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 (± 0.279) | 0.031 (± 0.2157) | | |
| Monocytes; Week 20; n= 61, 66 | 0.132 (± 0.2684) | 0.03 (± 0.1967) | | |
| Monocytes; Week 24; n= 61, 66 | 0.061 (± 0.229) | 0.013 (± 0.2412) | | |
| Monocytes; Week 28; n= 62, 65 | 0.107 (± 0.2363) | 0.035 (± 0.235) | | |
| 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) | 0.05 (± 0.2096) | | |
| Monocytes; Week 44; n= 59, 61 | 0.09 (± 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 (± 0.26) | 0.001 (± 0.2165) | | |
| Absolute Neutrophils; Baseline; n= 68, 68 | 7.5 (± 2.7424) | 7.198 (± 2.9732) | | |
| Neutrophils; Week 4; n= 66, 66 | -0.124 (± 2.617) | -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 | -0.56 (± 2.3679) | -1.243 (± 2.6857) | | |
| Neutrophils; Week 24; n= 61, 66 | -0.98 (± 2.3151) | -1.12 (± 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) | -1.01 (± 3.3999) | | |
| Neutrophils; Week 44; n= 59, 61 | -0.02 (± 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 (± 43.97) | 4.1 (± 26.48) | | |
| Platelets; Week 12; n= 63, 65 | 3.1 (± 50.6) | -4.3 (± 37.89) | | |
| Platelets; Week 16; n= 64, 68 | 15.4 (± 71.2) | 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 (± 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 (± 44.8) | | |
| 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 (± 48.51) | | |
| Platelets; Week 60; n= 59, 64 | 13 (± 50.07) | -2 (± 41.32) | | |

Notes:

[34] - Safety Population

[35] - 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[36] | 68[37] | | |
| 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 (± 6.6) | | |
| 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 (± 9.4) | | |
| MCHC; Week 48; n= 59, 64 | -6 (± 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 (± 9.9) | | |
| 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 (± 8.5) | -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 (± 8.2) | -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:

[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 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[38] | 68[39] | | |
| 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 (± 2.33) | | |
| Week 8; n= 66, 66 | 0.3 (± 2.5) | 0 (± 2.58) | | |
| Week 12; n= 63, 65 | 0.2 (± 2) | -0.7 (± 2.3) | | |
| Week 16; n= 64, 68 | 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 (± 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 (± 4.15) | | |
| Week 60; n= 59, 64 | -0.6 (± 6.57) | -1 (± 4.49) | | |

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 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[40] | 68[41] | | |
| 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 (± 0.95) | -0.16 (± 0.653) | | |
| Week 12; n= 63, 65 | -0.04 (± 0.55) | -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 (± 1.27) | -0.59 (± 0.959) | | |
| Week 28; n= 62, 66 | -0.51 (± 0.618) | -0.7 (± 1.184) | | |
| Week 32; n= 61, 67 | -0.66 (± 0.764) | -0.88 (± 1.368) | | |
| Week 36; n= 60, 66 | -0.6 (± 0.91) | -0.9 (± 1.395) | | |
| Week 40; n= 61, 65 | -0.67 (± 1.171) | -0.79 (± 1.39) | | |
| 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) | -0.8 (± 1.818) | | |

Notes:

[40] - Safety Population

[41] - 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[42] | 68[43] | | |
| Units: 10^12/ 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 (± 0.3) | 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 (± 0.27) | | |
| Week 44; n= 60, 64 | 0.13 (± 0.332) | 0.08 (± 0.26) | | |
| Week 48; n= 59, 64 | 0.14 (± 0.293) | 0.1 (± 0.271) | | |
| Week 52; n= 60, 64 | 0.1 (± 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:

[42] - Safety Population

[43] - 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[44] | 66[45] | | |
| Units: Participants | | | | |
| Negative | 66 | 65 | | |
| Positive | 1 | 1 | | |

Notes:

[44] - Safety Population

[45] - 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[46] | 68[47] | | |
| 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 (± 12.37) | | |
| SBP; Week 8; n= 67, 68 | 0.07 (± 14.192) | 1.29 (± 11.066) | | |
| SBP; Week 12; n= 66, 68 | -1.12 (± 14.38) | -1.41 (± 12.071) | | |
| SBP; Week 16; n= 64, 68 | -0.97 (± 16.63) | -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 (± 13.24) | | |
| 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 | 0.9 (± 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 (± 17.14) | -0.22 (± 12.351) | | |
| SBP: Week 52; n= 61, 65 | -1.03 (± 13.2) | -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 (± 10.13) | | |
| 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 (± 9.93) | -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 (± 10.57) | 0.11 (± 8.899) | | |
| DBP; Week 60; n= 61, 65 | -2.54 (± 11.278) | -0.45 (± 9.836) | | |

Notes:

[46] - Safety Population

[47] - 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[48] | 68[49] | | |
| 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 | 1.6 (± 11.703) | -0.31 (± 10.53) | | |
| 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 | 3.1 (± 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 | 2.6 (± 14.041) | -0.35 (± 9.986) | | |
| Week 60; n= 61, 65 | 1.51 (± 12.793) | 0.09 (± 10.28) | | |

Notes:

[48] - Safety Population

[49] - 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[50] | 68[51] | | |
| 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 (± 0.41) | -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 (± 0.53) | -0.13 (± 0.406) | | |
| Week 44; n= 61, 65 | -0.03 (± 0.55) | -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 (± 0.53) | 0 (± 0.402) | | |
| Week 60; n= 61, 64 | 0.03 (± 0.467) | -0.02 (± 0.479) | | |

Notes:

[50] - Safety Population

[51] - 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[52] | 68[53] | | |
| Units: milliseconds (msec) | | | | |
| arithmetic mean (standard deviation) | | | | |
| QTcF; Week 8; n= 66, 66 | 0.1 (± 17.9) | 1 (± 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 (± 15.96) | 3 (± 16.04) | | |
| QTcF; Week 60; n= 58, 63 | 3 (± 14.3) | 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 (± 18.1) | | |
| QTcB; Week 32; n= 61, 66 | 5.2 (± 29.63) | 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:

[52] - Safety Population

[53] - 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[54] | 68[55] | | |
| 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:

[54] - Safety Population

[55] - 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 | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | 0 / 68 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Weight increased | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | 1 / 68 (1.47%) | |
| occurrences (all) | 5 | 1 | |
| 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 | | | |
| Vertigo | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | 1 / 68 (1.47%) | |
| occurrences (all) | 5 | 1 | |
| Ear discomfort | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 4 / 68 (5.88%) | |
| occurrences (all) | 1 | 5 | |
| 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 | |

| | | | |
|---|---|---|---|
| Respiratory tract infection | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | 8 / 68 (11.76%) | |
| occurrences (all) | 7 | 15 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | 4 / 68 (5.88%) | |
| occurrences (all) | 5 | 6 | |
| 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