

**Clinical trial results:****An Open-Label Extension Study to evaluate the Long-Term Safety and Efficacy of Reslizumab (3.0 mg/kg) as Treatment for Patients with Eosinophilic Asthma who completed a prior Teva-Sponsored Study in Eosinophilic Asthma****Summary**

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2010-024540-15 |
| Trial protocol | BE DE SE CZ GR HU NL DK PL SK |
| Global end of trial date | 16 January 2015 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 19 April 2019 |
| First version publication date | 09 July 2016 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set To correct typo of country code Switzerland (CH) with Chile (CL) and correct the Philippines and Thailand patient counts (Philippines has 25 patients and Thailand 10 due to patient transfer). |

Trial information**Trial identification**

| | |
|-----------------------|-------------|
| Sponsor protocol code | C38072/3085 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01290887 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Teva Branded Pharmaceutical Products, R&D Inc. |
| Sponsor organisation address | 41 Moores Road, Frazer, Pennsylvania, United States, 19355 |
| Public contact | Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 215-591-3000, ustevatrials@tevapharm.com |
| Scientific contact | Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 215-591-3000, ustevatrials@tevapharm.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 June 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 January 2015 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety of reslizumab at a dosage of 3.0 mg/kg every 4 weeks for approximately 24 months in pediatric and adult patients with eosinophilic asthma as assessed by adverse events, physical examination findings, vital sign measurements, and concomitant medication usage throughout the study (every 4 weeks), clinical laboratory test results, and measurement of antidrug antibodies.

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (eg, Code of Federal Regulations Title 21, Parts 50, 54, 56, 312, and 314; European Union Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of GCP in the conduct of clinical studies of medicinal products for human use). Information regarding any investigational study centers participating in this study that could not comply with these standards was documented.

Written and/or oral information about the study was provided to all patients in a language understandable by the patients. The information included an adequate explanation of the aims, methods, anticipated benefits, potential hazards, and insurance arrangements in force. Written informed consent was obtained from each patient before any study procedures or assessments were done. It was explained to the patients that they were free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment.

For patients aged 12 to 17 years, a signed and dated informed consent form was obtained from a parent/guardian and a signed and dated assent form was obtained from each patient before any study-specific procedures or assessments were done and after the aims, methods, anticipated benefits, and potential hazards were explained, according to local IRB/IEC requirements.

Each patient's willingness to participate in the study was documented in writing in a consent/assent form that was signed by the patient and, in the case of patients aged 12 to 17 years, also signed by a parent/guardian, with the date of each signature indicated. Each investigator kept the original consent/assent forms, and copies were given to the patients.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 22 February 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 52 |
| Country: Number of subjects enrolled | Australia: 23 |
| Country: Number of subjects enrolled | Brazil: 37 |
| Country: Number of subjects enrolled | Canada: 16 |
| Country: Number of subjects enrolled | Israel: 57 |
| Country: Number of subjects enrolled | Korea, Republic of: 21 |
| Country: Number of subjects enrolled | Mexico: 36 |
| Country: Number of subjects enrolled | New Zealand: 16 |
| Country: Number of subjects enrolled | Peru: 55 |
| Country: Number of subjects enrolled | Philippines: 25 |
| Country: Number of subjects enrolled | Russian Federation: 69 |
| Country: Number of subjects enrolled | Thailand: 10 |
| Country: Number of subjects enrolled | Taiwan: 2 |
| Country: Number of subjects enrolled | Ukraine: 92 |
| Country: Number of subjects enrolled | United States: 160 |
| Country: Number of subjects enrolled | South Africa: 35 |
| Country: Number of subjects enrolled | Colombia: 17 |
| Country: Number of subjects enrolled | Malaysia: 17 |
| Country: Number of subjects enrolled | Poland: 59 |
| Country: Number of subjects enrolled | Romania: 16 |
| Country: Number of subjects enrolled | Slovakia: 27 |
| Country: Number of subjects enrolled | Sweden: 11 |
| Country: Number of subjects enrolled | Belgium: 37 |
| Country: Number of subjects enrolled | Czech Republic: 35 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Germany: 49 |
| Country: Number of subjects enrolled | Greece: 5 |
| Country: Number of subjects enrolled | Hungary: 46 |
| Country: Number of subjects enrolled | Chile: 14 |
| Worldwide total number of subjects | 1052 |
| EEA total number of subjects | 298 |

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) | 28 |
| Adults (18-64 years) | 921 |
| From 65 to 84 years | 103 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 1052 patients with eosinophilic asthma at 201 centers in 30 countries were enrolled in this study.

Pre-assignment

Screening details:

Four hundred-eighty (46%) patients received reslizumab for the first time in Study 3085, having previously received placebo in Studies 3081, 3082, or 3083.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|---|
| Arm title | Reslizumab 3.0 mg/kg |
| Arm description: | |
| Reslizumab 3.0 mg/kg administered intravenously once every 4 weeks (±7 days) for up to 24 months. | |
| Arm type | Experimental |
| Investigational medicinal product name | Reslizumab |
| Investigational medicinal product code | |
| Other name | Cinquil, humanized monoclonal antibody, CEP-38072 |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Reslizumab (3.0 mg/kg) administered intravenously by infusion every 28 days (±7 days), for approximately 24 months

| Number of subjects in period 1 | Reslizumab 3.0 mg/kg |
|------------------------------------|----------------------|
| Started | 1052 |
| Safety Analysis Set | 1051 |
| Completed | 50 |
| Not completed | 1002 |
| Adverse event, serious fatal | 3 |
| Non-compliance to study medication | 1 |
| Consent withdrawn by subject | 58 |
| Non-compliance to study procedures | 1 |
| Adverse event, non-fatal | 14 |
| Sponsor closure of the study | 896 |
| Not specified | 9 |
| Lost to follow-up | 8 |

| | |
|--------------------|---|
| Lack of efficacy | 9 |
| Protocol deviation | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Reslizumab 3.0 mg/kg |
|-----------------------|----------------------|

Reporting group description:

Reslizumab 3.0 mg/kg administered intravenously once every 4 weeks (+-7 days) for up to 24 months.

| Reporting group values | Reslizumab 3.0 mg/kg | Total | |
|---|----------------------|-------|--|
| Number of subjects | 1052 | 1052 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 47.2 | | |
| standard deviation | ± 14.02 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 646 | 646 | |
| Male | 406 | 406 | |
| Race | | | |
| Units: Subjects | | | |
| White | 808 | 808 | |
| Black | 44 | 44 | |
| Asian | 87 | 87 | |
| American Indian or Alaskan Native | 10 | 10 | |
| Pacific Islander | 2 | 2 | |
| Other | 101 | 101 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 201 | 201 | |
| Non-Hispanic or Latino | 365 | 365 | |
| Non-Hispanic and non-Latino | 480 | 480 | |
| Unknown | 6 | 6 | |
| Used Beta Agonist in Past 3 Days | | | |
| Usage of inhaled corticosteroids/long-acting beta-agonists and usage of oral corticosteroids. n=1051, 480, 571 | | | |
| Units: Subjects | | | |
| Yes | 597 | 597 | |

| | | | |
|--------------|-----|-----|--|
| No | 454 | 454 | |
| Not recorded | 1 | 1 | |

| | | | |
|--|-----------|---|--|
| Weight | | | |
| n=1021, 466, 555 | | | |
| Units: kg | | | |
| arithmetic mean | 76 | | |
| standard deviation | ± 17.32 | - | |
| Height | | | |
| n=1018, 463, 555 | | | |
| Units: cm | | | |
| arithmetic mean | 165.7 | | |
| standard deviation | ± 9.99 | - | |
| Body Mass Index | | | |
| n=1018, 463, 555 | | | |
| Units: kg/m ² | | | |
| arithmetic mean | 27.7 | | |
| standard deviation | ± 5.77 | - | |
| Forced Expiratory Volume in 1 Second (FEV1) | | | |
| Units: liters | | | |
| arithmetic mean | 2.199 | | |
| standard deviation | ± 0.8108 | - | |
| % Predicted Expiratory Volume In 1 Second | | | |
| Units: percentage of predicted FEV1 | | | |
| arithmetic mean | 73.115 | | |
| standard deviation | ± 19.9664 | - | |
| Forced Vital Capacity (FVC) | | | |
| Units: liters | | | |
| arithmetic mean | 3.273 | | |
| standard deviation | ± 1.0632 | - | |
| Forced Expiratory Flow at 25% to 75% Forced Vital Capacity (FEF 25%-75%) | | | |
| n=1046, 478, 568 | | | |
| Units: liters/second | | | |
| arithmetic mean | 1.558 | | |
| standard deviation | ± 0.9009 | - | |
| Asthma Control Questionnaire (ACQ) | | | |
| The ACQ is a 7-item instrument that measures asthma control (Juniper et al 1999). Six questions are self-assessments; the seventh item, completed by a member of the study staff, is the result of the patient's FEV1 measurement. Each item has 7 possible answers on a scale of 0 to 6, and the total score is the mean of all responses (the total scale is therefore 0-6). A higher score is an indication of poorer asthma control. n=1051, 480, 571 | | | |
| Units: units on a scale | | | |
| arithmetic mean | 1.624 | | |
| standard deviation | ± 1.0527 | - | |
| Asthma Quality of Life Questionnaire (AQLQ) | | | |
| The AQLQ is a 32-item instrument administered as a self-assessment (Juniper et al 1992). The questionnaire is divided into 4 domains: activity limitation, symptoms, emotional function, and environmental stimuli. Patients were asked to recall their experiences during the last 2 weeks and to respond to each question on a 7-point scale (1=severe impairment, 7=no impairment). The overall AQLQ score is the mean of all 32 responses. n=1045, 476, 569 | | | |

| | | | |
|---|-------------------|---|--|
| Units: units on a scale arithmetic mean standard deviation | 5.347 ± 1.1875 | - | |
| Asthma Symptom Utility Index (ASUI) | | | |
| The ASUI is an 11-item instrument designed to assess the frequency and severity of asthma symptoms and side effects, weighted by patient preferences (Revicki et al 1998). ASUI is a utility score that ranges from 0 to 1, with higher values indicating better asthma control. n=377, 186, 191 | | | |
| Units: units on a scale arithmetic mean standard deviation | 0.832 ± 0.1728 | - | |
| Blood Eosinophil Count | | | |
| Units: 10 ⁹ /liter arithmetic mean standard deviation | 0.284 ± 0.3577 | - | |
| Daily average number of puffs in past 3 days | | | |
| n=1029, 475, 554 | | | |
| Units: puffs arithmetic mean standard deviation | 1.827 ± 2.4604 | - | |

Subject analysis sets

| | |
|----------------------------|--|
| Subject analysis set title | Previous Placebo-Treated Subpopulation |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The subpopulation of participants who were treated with placebo in the previous double-blind studies. These participants were treated with reslizumab 3.0 mg/kg intravenously once every 4 weeks (+ -7 days) for up to 24 months in this study.

| | |
|----------------------------|---|
| Subject analysis set title | Previous Reslizumab-Treated Subpopulation |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The subpopulation of participants who were treated with reslizumab at a variety of dosages in the previous double-blind studies. These participants were treated with reslizumab 3.0 mg/kg intravenously once every 4 weeks (+ -7 days) for up to 24 months in this study.

| Reporting group values | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|---|--|---|--|
| Number of subjects | 481 | 571 | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |

| | | | |
|---|-------------------|-------------------|--|
| Age continuous Units: years arithmetic mean standard deviation | 47.4 ± 14.53 | 47.1 ± 13.58 | |
| Gender categorical Units: Subjects | | | |
| Female | 314 | 332 | |
| Male | 167 | 239 | |
| Race Units: Subjects | | | |
| White | 371 | 437 | |
| Black | 22 | 22 | |
| Asian | 39 | 48 | |
| American Indian or Alaskan Native | 4 | 6 | |
| Pacific Islander | 1 | 1 | |
| Other | 44 | 57 | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 83 | 118 | |
| Non-Hispanic or Latino | 187 | 178 | |
| Non-Hispanic and non-Latino | 208 | 272 | |
| Unknown | 3 | 3 | |
| Used Beta Agonist in Past 3 Days | | | |
| Usage of inhaled corticosteroids/long-acting beta-agonists and usage of oral corticosteroids. n=1051, 480, 571 | | | |
| Units: Subjects | | | |
| Yes | 300 | 297 | |
| No | 180 | 274 | |
| Not recorded | 1 | 1 | |
| Weight n=1021, 466, 555 | | | |
| Units: kg arithmetic mean standard deviation | 75.4 ± 16.67 | 76.5 ± 17.85 | |
| Height n=1018, 463, 555 | | | |
| Units: cm arithmetic mean standard deviation | 165.3 ± 10.03 | 166 ± 9.96 | |
| Body Mass Index n=1018, 463, 555 | | | |
| Units: kg/m ² arithmetic mean standard deviation | 27.6 ± 5.42 | 27.7 ± 6.04 | |
| Forced Expiratory Volume in 1 Second (FEV1) Units: liters arithmetic mean standard deviation | 2.096 ± 0.7856 | 2.285 ± 0.8222 | |
| % Predicted Expiratory Volume In 1 Second Units: percentage of predicted FEV1 | | | |

| | | | |
|--|----------|-----------|--|
| arithmetic mean | 70.739 | 75.116 | |
| standard deviation | ± 19.756 | ± 19.9404 | |
| Forced Vital Capacity (FVC) | | | |
| Units: liters | | | |
| arithmetic mean | 3.163 | 3.366 | |
| standard deviation | ± 1.0357 | ± 1.0779 | |
| Forced Expiratory Flow at 25% to 75% Forced Vital Capacity (FEF 25%-75%) | | | |
| n=1046, 478, 568 | | | |
| Units: liters/second | | | |
| arithmetic mean | 1.467 | 1.634 | |
| standard deviation | ± 0.889 | ± 0.9045 | |
| Asthma Control Questionnaire (ACQ) | | | |
| The ACQ is a 7-item instrument that measures asthma control (Juniper et al 1999). Six questions are self-assessments; the seventh item, completed by a member of the study staff, is the result of the patient's FEV1 measurement. Each item has 7 possible answers on a scale of 0 to 6, and the total score is the mean of all responses (the total scale is therefore 0-6). A higher score is an indication of poorer asthma control. n=1051, 480, 571 | | | |
| Units: units on a scale | | | |
| arithmetic mean | 1.832 | 1.45 | |
| standard deviation | ± 1.0912 | ± 0.987 | |
| Asthma Quality of Life Questionnaire (AQLQ) | | | |
| The AQLQ is a 32-item instrument administered as a self-assessment (Juniper et al 1992). The questionnaire is divided into 4 domains: activity limitation, symptoms, emotional function, and environmental stimuli. Patients were asked to recall their experiences during the last 2 weeks and to respond to each question on a 7-point scale (1=severe impairment, 7=no impairment). The overall AQLQ score is the mean of all 32 responses. n=1045, 476, 569 | | | |
| Units: units on a scale | | | |
| arithmetic mean | 5.17 | 5.496 | |
| standard deviation | ± 1.216 | ± 1.1431 | |
| Asthma Symptom Utility Index (ASUI) | | | |
| The ASUI is an 11-item instrument designed to assess the frequency and severity of asthma symptoms and side effects, weighted by patient preferences (Revicki et al 1998). ASUI is a utility score that ranges from 0 to 1, with higher values indicating better asthma control. n=377, 186, 191 | | | |
| Units: units on a scale | | | |
| arithmetic mean | 0.803 | 0.861 | |
| standard deviation | ± 0.191 | ± 0.1479 | |
| Blood Eosinophil Count | | | |
| Units: 10 ⁹ /liter | | | |
| arithmetic mean | 0.528 | 0.078 | |
| standard deviation | ± 0.3792 | ± 0.148 | |
| Daily average number of puffs in past 3 days | | | |
| n=1029, 475, 554 | | | |
| Units: puffs | | | |
| arithmetic mean | 2.13 | 1.568 | |
| standard deviation | ± 2.4996 | ± 2.3982 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Reslizumab 3.0 mg/kg |
| Reporting group description: Reslizumab 3.0 mg/kg administered intravenously once every 4 weeks (+-7 days) for up to 24 months. | |
| Subject analysis set title | Previous Placebo-Treated Subpopulation |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The subpopulation of participants who were treated with placebo in the previous double-blind studies. These participants were treated with reslizumab 3.0 mg/kg intravenously once every 4 weeks (+-7 days) for up to 24 months in this study. | |
| Subject analysis set title | Previous Reslizumab-Treated Subpopulation |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The subpopulation of participants who were treated with reslizumab at a variety of dosages in the previous double-blind studies. These participants were treated with reslizumab 3.0 mg/kg intravenously once every 4 weeks (+-7 days) for up to 24 months in this study. | |

Primary: Participants With Treatment-Emergent Adverse Events

| | |
|---|--|
| End point title | Participants With Treatment-Emergent Adverse Events ^[1] |
| End point description: An adverse event was defined in the protocol as any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to the study drug. Severity was rated by the investigator on a scale of mild, moderate and severe, with severe= an inability to carry out usual activities. Relation of AE to treatment was determined by the investigator. Serious AEs include death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, OR an important medical event that jeopardized the patient and required medical intervention to prevent the previously listed serious outcomes. | |
| End point type | Primary |
| End point timeframe: Day 1 (post-dose) to Week 65. The endpoint for adverse events was the last postbaseline observation, which included the 90 day follow-up visit. | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Single treatment arm study. No analysis was planned to compare the subpopulations.

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[2] | 480 ^[3] | 571 ^[4] | |
| Units: participants | | | | |
| At least 1 AE | 744 | 359 | 385 | |
| Severe AE | 78 | 31 | 47 | |
| Treatment-related AE | 90 | 49 | 41 | |
| AE causing patient discontinuation | 18 | 6 | 12 | |
| Serious AE | 78 | 33 | 45 | |
| Death | 3 | 1 | 2 | |
| AE up to follow-up period | 711 | 344 | 367 | |
| AE during follow-up period | 160 | 78 | 82 | |

Notes:

[2] - Safety analysis set

[3] - Safety analysis set

[4] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Participants With Treatment-Emergent Potentially Clinically Significant (PCS) Abnormal Lab Values

| | |
|-----------------|--|
| End point title | Participants With Treatment-Emergent Potentially Clinically Significant (PCS) Abnormal Lab Values ^[5] |
|-----------------|--|

End point description:

Participants with potentially clinically significant (PCS) abnormal serum chemistry, hematology, and urinalysis values on any of the during treatment lab analyses.

Significance criteria:

- Blood urea nitrogen: ≥ 10.71 mmol/L
- Creatinine: ≥ 177 μ mol/L
- Uric acid: M ≥ 625 , F ≥ 506 μ mol/L
- Aspartate aminotransferase: $\geq 3 \times$ upper limit of normal (ULN). Normal range is 10-43 U/L
- Alanine aminotransferase: $\geq 3 \times$ ULN. Normal range is 10-40 U/L
- GGT = gamma-glutamyl transpeptidase: $\geq 3 \times$ upper limit of normal. Normal range is 5-49 U/L.
- Total bilirubin: ≥ 34.2 μ mol/L
- White blood cells- low: $\leq 3.0 \times 10^9$ /L
- White blood cells-high: $\geq 20 \times 10^9$ /L
- Hemoglobin: M ≤ 115 , F ≤ 95 g/dL
- Hematocrit: M ≤ 0.37 , F ≤ 0.32 L/L
- Platelets: $\geq 700 \times 10^9$ /L
- Absolute neutrophil count: $\leq 1.0 \times 10^9$ /L
- Eosinophils: ≥ 10
- Urinalysis: ketones, blood, glucose, and total protein: ≥ 2 unit increase from baseline

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Weeks 4, 8, 24 and 48

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Single treatment arm study. No analysis was planned to compare the subpopulations.

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|-----------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1044 ^[6] | 477 ^[7] | 567 ^[8] | |
| Units: participants | | | | |
| Blood urea nitrogen | 23 | 13 | 10 | |
| Creatinine | 5 | 3 | 2 | |
| Uric acid | 13 | 8 | 5 | |
| Aspartate aminotransferase | 11 | 6 | 5 | |
| Alanine aminotransferase | 14 | 7 | 7 | |
| GGT | 39 | 24 | 15 | |
| Total bilirubin | 6 | 3 | 3 | |
| White blood cells- low | 18 | 10 | 8 | |
| White blood cells- high | 3 | 2 | 1 | |

| | | | | |
|-----------------------------|-----|----|----|--|
| Hemoglobin | 19 | 10 | 9 | |
| Hematocrit | 26 | 13 | 13 | |
| Platelets | 2 | 1 | 1 | |
| Absolute neutrophil count | 14 | 7 | 7 | |
| Eosinophils | 51 | 24 | 27 | |
| Ketones in urine | 24 | 15 | 9 | |
| Blood (hemoglobin) in urine | 107 | 52 | 55 | |
| Glucose in urine | 54 | 22 | 32 | |
| Total protein in urine | 156 | 71 | 85 | |

Notes:

[6] - Safety analysis set, including participants who contributed to the analysis

[7] - Safety analysis set, including participants who contributed to the analysis

[8] - Safety analysis set, including participants who contributed to the analysis

Statistical analyses

No statistical analyses for this end point

Primary: Participants With Treatment-Emergent Potentially Clinically Significant (PCS) Vital Signs Values

| | |
|-----------------|---|
| End point title | Participants With Treatment-Emergent Potentially Clinically Significant (PCS) Vital Signs Values ^[9] |
|-----------------|---|

End point description:

Significance criteria

- Sitting heart rate-high: >100 and increase of ≥ 30 beats/min (all ages)
- Sitting heart rate-low: <50 and decrease of ≥ 30 beats/min
- Systolic blood pressure (BP)-high: >130 and increase of ≥ 30 mmHg (ages 12-17)
- Systolic BP-low: <90 and decrease of ≥ 30 mmHg (ages ≥ 18)
- Systolic BP-high: >160 and increase of ≥ 30 mmHg (ages ≥ 18)
- Diastolic BP-low: <55 and decrease of ≥ 12 mmHg (ages 12-17)
- Diastolic BP-high: >85 and increase of ≥ 12 mmHg (ages 12-17)
- Diastolic BP-low: <50 and decrease of ≥ 12 mmHg (ages ≥ 18)
- Diastolic BP-high: >100 and increase of ≥ 12 mmHg (ages ≥ 18)
- Respiration rate: >20 and increase of ≥ 10 breaths/minute (ages 12-17)
- Respiration rate: >24 and increase of ≥ 10 breaths/minute (ages ≥ 18)
- Body temperature-low: <96.5° Fahrenheit (all ages)
- Body temp-high: >100.5° F (all ages)

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 4 to Week 65 (treatment and follow-up visits)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Single treatment arm study. No analysis was planned to compare the subpopulations.

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|-------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1047 ^[10] | 478 ^[11] | 571 ^[12] | |
| Units: participants | | | | |
| Heart rate - high (ages 12-17) | 3 | 1 | 2 | |
| Heart rate - low (ages ≥ 18) | 3 | 2 | 1 | |
| Heart rate - high (ages ≥ 18) | 16 | 8 | 8 | |
| Systolic BP - high (ages 12-17) | 1 | 0 | 1 | |

| | | | | |
|--------------------------------------|-----|-----|-----|--|
| Systolic BP - low (ages >=18) | 1 | 1 | 0 | |
| Systolic BP - high (ages >=18) | 16 | 8 | 8 | |
| Diastolic BP - low (ages 12-17) | 2 | 1 | 1 | |
| Diastolic BP - high (ages 12-17) | 3 | 2 | 1 | |
| Diastolic BP - low (ages >=18) | 6 | 2 | 4 | |
| Diastolic - high (ages >=18) | 25 | 13 | 12 | |
| Respiration rate - high (ages 12-17) | 1 | 0 | 1 | |
| Respiration rate - high (ages >=18) | 8 | 6 | 2 | |
| Body temperature - low (ages 12-17) | 6 | 3 | 3 | |
| Body temperature - high (ages 12-17) | 1 | 0 | 1 | |
| Body temperature - low (ages >=18) | 223 | 102 | 121 | |
| Body temperature - high (ages >=18) | 4 | 3 | 1 | |

Notes:

[10] - Safety analysis set, including participants who contributed to the analysis

[11] - Safety analysis set, including participants who contributed to the analysis

[12] - Safety analysis set, including participants who contributed to the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume In 1 Second (FEV1) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Forced Expiratory Volume In 1 Second (FEV1) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

FEV1 is a standard measurement of air movement in the lungs of patients with asthma obtained from pulmonary function tests. It is the volume of air expired in the first second of a forced expiration using a spirometer.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[13] | 480 ^[14] | 571 ^[15] | |
| Units: liters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=1009, 457, 552) | 2.222 (± 0.7857) | 2.155 (± 0.7636) | 2.277 (± 0.7999) | |
| Week 8 (n=955, 437, 518) | 2.22 (± 0.8096) | 2.162 (± 0.7966) | 2.27 (± 0.8179) | |
| Week 12 (n=925, 426, 499) | 2.223 (± 0.7932) | 2.171 (± 0.769) | 2.267 (± 0.8114) | |
| Week 16 (n=906, 418, 488) | 2.222 (± 0.7957) | 2.169 (± 0.7761) | 2.267 (± 0.8101) | |
| Week 24 (n=844, 386, 458) | 2.243 (± 0.8013) | 2.188 (± 0.7966) | 2.289 (± 0.8032) | |

| | | | | |
|-----------------------------|------------------|------------------|------------------|--|
| Week 36 (n=645, 291, 354) | 2.258 (± 0.8178) | 2.234 (± 0.824) | 2.278 (± 0.8133) | |
| Week 48 (n=448, 198, 250) | 2.261 (± 0.8099) | 2.167 (± 0.7905) | 2.336 (± 0.8189) | |
| Week 60 (n=244, 101, 143) | 2.308 (± 0.8689) | 2.234 (± 0.9214) | 2.36 (± 0.8292) | |
| Week 72 (n=161, 56, 105) | 2.387 (± 0.8466) | 2.424 (± 0.9093) | 2.367 (± 0.815) | |
| Week 84 (n=133, 45, 88) | 2.422 (± 0.8425) | 2.496 (± 0.8496) | 2.384 (± 0.8411) | |
| Week 96 (n=69, 23, 46) | 2.505 (± 0.8283) | 2.748 (± 0.8963) | 2.383 (± 0.7737) | |
| End of study (n=82, 28, 54) | 2.329 (± 0.8997) | 2.505 (± 0.9386) | 2.237 (± 0.8736) | |
| Endpoint (n=1047, 478, 569) | 2.228 (± 0.7989) | 2.174 (± 0.7798) | 2.273 (± 0.8127) | |

Notes:

[13] - Safety analysis set of participants with assessments at stated timeframes

[14] - Safety analysis set of participants with assessments at stated timeframes

[15] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Predicted Forced Expiratory Volume In 1 Second (% Predicted FEV1) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Percent Predicted Forced Expiratory Volume In 1 Second (% Predicted FEV1) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

The percent predicted FEV1 is the ratio of the volume of air expired in the first second of a forced expiration to the patient's predicted FEV based on a similar population without asthma. Percent predicted lung function values were transcribed directly from the lung function report to the CRF, without any calculation by Teva.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[16] | 480 ^[17] | 571 ^[18] | |
| Units: percentage of predicted FEV1 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=1009, 457, 552) | 74.123 (± 19.4521) | 73.295 (± 19.7933) | 74.808 (± 19.156) | |
| Week 8 (n=955, 437, 518) | 73.983 (± 20.1949) | 73.056 (± 19.9848) | 74.765 (± 20.357) | |
| Week 12 (n=925, 426, 499) | 74.279 (± 19.6002) | 73.797 (± 19.2586) | 74.69 (± 19.8973) | |
| Week 16 (n=906, 418, 488) | 74.266 (± 19.9188) | 73.797 (± 19.5962) | 74.668 (± 20.2025) | |

| | | | | |
|-----------------------------|--------------------|--------------------|--------------------|--|
| Week 24 (n=844, 386, 458) | 74.785 (± 19.7729) | 74.284 (± 19.5601) | 75.208 (± 19.9621) | |
| Week 36 (n=645, 291, 354) | 75.179 (± 20.493) | 74.805 (± 20.5634) | 75.487 (± 20.4589) | |
| Week 48 (n=448, 198, 250) | 75.313 (± 19.95) | 73.654 (± 19.9535) | 76.627 (± 19.889) | |
| Week 60 (n=244, 101, 143) | 75.743 (± 21.195) | 74.511 (± 22.5211) | 76.613 (± 20.2416) | |
| Week 72 (n=161, 56, 105) | 76.827 (± 18.2256) | 76.856 (± 20.1821) | 76.812 (± 17.1937) | |
| Week 84 (n=133, 45, 88) | 78.308 (± 18.4011) | 79.017 (± 18.5149) | 77.945 (± 18.4383) | |
| Week 96 (n=69, 23, 46) | 78.912 (± 15.9949) | 83.245 (± 14.9074) | 76.746 (± 16.2345) | |
| End of study (n=82, 28, 54) | 73.719 (± 20.0902) | 79.672 (± 18.6997) | 70.633 (± 20.2554) | |
| Endpoint (n=1047, 478, 569) | 74.69 (± 19.8307) | 74.195 (± 19.8134) | 75.107 (± 19.853) | |

Notes:

[16] - Safety analysis set of participants with assessments at stated timeframes

[17] - Safety analysis set of participants with assessments at stated timeframes

[18] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Vital Capacity (FVC) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Forced Vital Capacity (FVC) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

The FVC is the volume of air that can be forcibly blown out after full inspiration, measured in liters.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[19] | 480 ^[20] | 571 ^[21] | |
| Units: liters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=1009, 457, 552) | 3.304 (± 1.0334) | 3.222 (± 0.9929) | 3.372 (± 1.0619) | |
| Week 8 (n=955, 437, 518) | 3.297 (± 1.0577) | 3.226 (± 1.0228) | 3.358 (± 1.0836) | |
| Week 12 (n=925, 426, 499) | 3.292 (± 1.0232) | 3.238 (± 0.9788) | 3.339 (± 1.0584) | |
| Week 16 (n=906, 418, 488) | 3.298 (± 1.0444) | 3.238 (± 0.9949) | 3.349 (± 1.0835) | |
| Week 24 (n=844, 386, 458) | 3.307 (± 1.0449) | 3.233 (± 1.0095) | 3.369 (± 1.0709) | |

| | | | | |
|-----------------------------|------------------|------------------|------------------|--|
| Week 36 (n=644, 291, 353) | 3.336 (± 1.0479) | 3.324 (± 1.0571) | 3.346 (± 1.0416) | |
| Week 48 (n=448, 198, 250) | 3.332 (± 1.0371) | 3.229 (± 1.0334) | 3.414 (± 1.0348) | |
| Week 60 (n=244, 101, 143) | 3.381 (± 1.1037) | 3.323 (± 1.1874) | 3.422 (± 1.0428) | |
| Week 72 (n=161, 56, 105) | 3.434 (± 1.1143) | 3.5 (± 1.1839) | 3.398 (± 1.0795) | |
| Week 84 (n=133, 45, 88) | 3.474 (± 1.1487) | 3.606 (± 1.1403) | 3.406 (± 1.1535) | |
| Week 96 (n=69, 23, 46) | 3.537 (± 1.168) | 3.849 (± 1.2342) | 3.381 (± 1.1145) | |
| End of study (n=82, 28, 54) | 3.39 (± 1.2206) | 3.524 (± 1.1842) | 3.321 (± 1.2443) | |
| Endpoint (n=1047, 478, 569) | 3.307 (± 1.0466) | 3.25 (± 1.0194) | 3.355 (± 1.0675) | |

Notes:

[19] - Safety analysis set of participants with assessments at stated timeframes

[20] - Safety analysis set of participants with assessments at stated timeframes

[21] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Flow at 25% to 75% Forced Vital Capacity (FEF 25%-75%) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|---|
| End point title | Forced Expiratory Flow at 25% to 75% Forced Vital Capacity (FEF 25%-75%) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|---|

End point description:

The FEF 25%-75% is the force expiratory flow at 25% to 75% of the Forced Vital Capacity (FVC), measured in liters/second.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[22] | 480 ^[23] | 571 ^[24] | |
| Units: liters/second | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=991, 446, 545) | 1.589 (± 0.9195) | 1.558 (± 0.9363) | 1.614 (± 0.9055) | |
| Week 8 (n=942, 429, 513) | 1.585 (± 0.9268) | 1.546 (± 0.9279) | 1.618 (± 0.9255) | |
| Week 12 (n=912, 418, 494) | 1.607 (± 0.958) | 1.587 (± 0.9833) | 1.624 (± 0.9367) | |
| Week 16 (n=891, 408, 483) | 1.593 (± 0.9234) | 1.561 (± 0.9427) | 1.62 (± 0.9068) | |
| Week 24 (n=830, 377, 453) | 1.629 (± 0.9565) | 1.619 (± 0.9967) | 1.637 (± 0.9227) | |

| | | | | |
|-----------------------------|------------------|------------------|------------------|--|
| Week 36 (n=634, 285, 349) | 1.646 (± 1.008) | 1.642 (± 1.1087) | 1.65 (± 0.9193) | |
| Week 48 (n=440, 191, 249) | 1.664 (± 0.9871) | 1.628 (± 1.0408) | 1.691 (± 0.945) | |
| Week 60 (n=242, 99, 143) | 1.715 (± 1.1265) | 1.605 (± 1.0869) | 1.791 (± 1.1508) | |
| Week 72 (n=161, 56, 105) | 1.781 (± 1.0276) | 1.81 (± 1.0239) | 1.766 (± 1.0341) | |
| Week 84 (n=133, 45, 88) | 1.877 (± 1.07) | 1.848 (± 0.9047) | 1.892 (± 1.1499) | |
| Week 96 (n=69, 23, 46) | 2.001 (± 1.0457) | 2.12 (± 1.0597) | 1.942 (± 1.0453) | |
| End of study (n=82, 28, 54) | 1.741 (± 0.9854) | 1.939 (± 1.1105) | 1.639 (± 0.9079) | |
| Endpoint (n=1031, 468, 563) | 1.592 (± 0.9188) | 1.546 (± 0.9041) | 1.629 (± 0.93) | |

Notes:

[22] - Safety analysis set of participants with assessments at stated timeframes

[23] - Safety analysis set of participants with assessments at stated timeframes

[24] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Average Daily Use of Short-Acting Beta-Agonist (SABA) Therapy at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Average Daily Use of Short-Acting Beta-Agonist (SABA) Therapy at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

SABA are used for quick relief of asthma symptoms. To measure SABA use, at each clinical visit participants were asked to recall their usage of SABA therapy within the last 3 days of the scheduled visit. If usage was confirmed, the number of puffs used was recorded. For the purpose of summaries, an average daily usage was evaluated by dividing the total number of puffs recorded over 3 days by 3.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[25] | 480 ^[26] | 571 ^[27] | |
| Units: # puffs/day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=599, 276, 323) | 2.5 (± 2.43) | 2.5 (± 2.42) | 2.4 (± 2.45) | |
| Week 8 (n=560, 258, 302) | 2.4 (± 2.46) | 2.4 (± 2.28) | 2.4 (± 2.62) | |
| Week 12 (n=529, 251, 278) | 2.5 (± 2.3) | 2.6 (± 2.07) | 2.4 (± 2.5) | |
| Week 16 (n=505, 244, 261) | 2.4 (± 2.3) | 2.5 (± 2.3) | 2.2 (± 2.29) | |
| Week 24 (n=454, 211, 243) | 2.4 (± 2.51) | 2.6 (± 2.55) | 2.3 (± 2.46) | |
| Week 36 (n=334, 160, 174) | 2.3 (± 2.47) | 2.4 (± 2.27) | 2.3 (± 2.64) | |
| Week 48 (n=232, 111, 121) | 2.3 (± 2.42) | 2.2 (± 2.28) | 2.4 (± 2.54) | |

| | | | | |
|-----------------------------|--------------|--------------|--------------|--|
| Week 60 (n=114, 50, 64) | 2.3 (± 2.86) | 2.1 (± 2.19) | 2.5 (± 3.3) | |
| Week 72 (n=76, 29, 47) | 1.9 (± 1.99) | 2.1 (± 2.19) | 1.8 (± 1.88) | |
| Week 84 (n=54, 19, 35) | 2.2 (± 2.12) | 2 (± 1.57) | 2.4 (± 2.38) | |
| Week 96 (n=40, 14, 26) | 1.8 (± 1.5) | 1.8 (± 1.41) | 1.7 (± 1.57) | |
| End of study (n=39, 16, 23) | 2.4 (± 1.9) | 2.1 (± 1.76) | 2.7 (± 1.99) | |
| Endpoint (n=843, 390, 453) | 2.2 (± 3.35) | 2.2 (± 2.2) | 2.2 (± 4.09) | |

Notes:

[25] - Safety analysis set of participants with assessments at stated timeframes

[26] - Safety analysis set of participants with assessments at stated timeframes

[27] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Symptom Utility Index (ASUI) Score at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Asthma Symptom Utility Index (ASUI) Score at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

The ASUI is an 11-item instrument designed to assess the frequency and severity of asthma symptoms and side effects, weighted by patient preferences (Revicki et al 1998). ASUI is a utility score that ranges from 0 to 1, with higher values indicating better asthma control.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[28] | 480 ^[29] | 571 ^[30] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=1008, 456, 552) | 0.838 (± 0.1724) | 0.831 (± 0.1829) | 0.844 (± 0.1631) | |
| Week 8 (n=950, 436, 514) | 0.847 (± 0.1626) | 0.843 (± 0.1663) | 0.851 (± 0.1596) | |
| Week 12 (n=926, 426, 500) | 0.847 (± 0.1661) | 0.839 (± 0.1752) | 0.854 (± 0.1578) | |
| Week 16 (n=902, 416, 486) | 0.851 (± 0.1673) | 0.845 (± 0.169) | 0.856 (± 0.1659) | |
| Week 24 (n=844, 386, 458) | 0.852 (± 0.1658) | 0.844 (± 0.172) | 0.859 (± 0.1602) | |
| Week 36 (n=645, 291, 354) | 0.857 (± 0.1673) | 0.844 (± 0.1821) | 0.867 (± 0.1536) | |
| Week 48 (n=449, 198, 251) | 0.854 (± 0.1701) | 0.851 (± 0.1699) | 0.856 (± 0.1705) | |
| Week 60 (n=246, 100, 146) | 0.866 (± 0.1534) | 0.869 (± 0.1573) | 0.865 (± 0.1513) | |
| Week 72 (n=161, 56, 105) | 0.865 (± 0.1453) | 0.876 (± 0.1346) | 0.858 (± 0.1509) | |

| | | | | |
|-----------------------------|------------------|------------------|------------------|--|
| Week 84 (n=132, 45, 87) | 0.873 (± 0.151) | 0.884 (± 0.146) | 0.868 (± 0.1541) | |
| Week 96 (n=69, 23, 46) | 0.832 (± 0.1823) | 0.822 (± 0.2036) | 0.836 (± 0.1729) | |
| End of study (n=83, 28, 55) | 0.853 (± 0.1767) | 0.877 (± 0.0979) | 0.84 (± 0.2053) | |
| Endpoint (n=1047, 478, 569) | 0.847 (± 0.1669) | 0.843 (± 0.1679) | 0.85 (± 0.1661) | |

Notes:

[28] - Safety analysis set of participants with assessments at stated timeframes

[29] - Safety analysis set of participants with assessments at stated timeframes

[30] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Control Questionnaire (ACQ) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint

| | |
|-----------------|---|
| End point title | Asthma Control Questionnaire (ACQ) at Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, End of Study and Endpoint |
|-----------------|---|

End point description:

The ACQ is a 7-item instrument that measures asthma control (Juniper et al 1999). Six questions are self-assessments; the seventh item, completed by a member of the study staff, is the result of the patient's FEV1 measurement. Each item has 7 possible answers on a scale of 0 to 6, and the total score is the mean of all responses (the total scale is therefore 0-6). A higher score is an indication of poorer asthma control.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96, end of study and endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[31] | 480 ^[32] | 571 ^[33] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=1008, 456, 552) | 1.482 (± 0.9852) | 1.546 (± 1.0154) | 1.429 (± 0.9573) | |
| Week 8 (n=954, 437, 517) | 1.417 (± 0.9762) | 1.446 (± 0.9805) | 1.392 (± 0.9729) | |
| Week 12 (n=926, 426, 500) | 1.405 (± 0.9648) | 1.459 (± 1.0004) | 1.36 (± 0.932) | |
| Week 16 (n=903, 416, 487) | 1.369 (± 0.9655) | 1.444 (± 1.0016) | 1.305 (± 0.9299) | |
| Week 24 (n=844, 386, 458) | 1.362 (± 0.9812) | 1.436 (± 1.0135) | 1.299 (± 0.9497) | |
| Week 36 (n=644, 291, 353) | 1.347 (± 0.9746) | 1.425 (± 1.0189) | 1.282 (± 0.9331) | |
| Week 48 (n=448, 198, 250) | 1.346 (± 0.9766) | 1.408 (± 0.9699) | 1.297 (± 0.981) | |
| Week 60 (n=243, 100, 143) | 1.292 (± 0.954) | 1.284 (± 0.9739) | 1.297 (± 0.9432) | |

| | | | | |
|-----------------------------|------------------|------------------|------------------|--|
| Week 72 (n=161, 56, 105) | 1.249 (± 0.8587) | 1.283 (± 0.9176) | 1.231 (± 0.8295) | |
| Week 84 (n=132, 45, 87) | 1.186 (± 0.91) | 1.143 (± 0.902) | 1.209 (± 0.9186) | |
| Week 96 (n=69, 23, 46) | 1.369 (± 0.9594) | 1.323 (± 0.9862) | 1.391 (± 0.9559) | |
| End of study (n=82, 28, 54) | 1.308 (± 0.9216) | 1.061 (± 0.7653) | 1.437 (± 0.975) | |
| Endpoint (n=1047, 478, 569) | 1.417 (± 0.9759) | 1.45 (± 0.9901) | 1.389 (± 0.9637) | |

Notes:

[31] - Safety analysis set of participants with assessments at stated timeframes

[32] - Safety analysis set of participants with assessments at stated timeframes

[33] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Quality of Life Questionnaire (AQLQ) Total Score at Weeks 24, 48, 72, 96, End of Study and Endpoint

| | |
|-----------------|--|
| End point title | Asthma Quality of Life Questionnaire (AQLQ) Total Score at Weeks 24, 48, 72, 96, End of Study and Endpoint |
|-----------------|--|

End point description:

The AQLQ is a 32-item instrument administered as a self-assessment (Juniper et al 1992). The questionnaire is divided into 4 domains: activity limitation, symptoms, emotional function, and environmental stimuli. Patients were asked to recall their experiences during the last 2 weeks and to respond to each question on a 7-point scale (1=severe impairment, 7=no impairment). The overall AQLQ score is the mean of all 32 responses. Five of the activity questions were "patient-specific," which means that each patient identified and scored 5 activities in which the patient was limited by asthma; these 5 activities were identified at the first visit and retained for all subsequent follow-up visits.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 24, 48, 72, 96, End of Study and Endpoint

| End point values | Reslizumab 3.0 mg/kg | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | |
|--------------------------------------|----------------------|--|---|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1051 ^[34] | 480 ^[35] | 571 ^[36] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n=834, 382, 452) | 5.627 (± 1.1091) | 5.551 (± 1.1558) | 5.691 (± 1.0651) | |
| Week 48 (n=442, 193, 249) | 5.672 (± 1.0982) | 5.602 (± 1.118) | 5.725 (± 1.0818) | |
| Week 72 (n=162, 56, 106) | 5.809 (± 1.0124) | 5.808 (± 1.0002) | 5.809 (± 1.0235) | |
| Week 96 (n=69, 23, 46) | 5.734 (± 1.1333) | 5.585 (± 1.1422) | 5.809 (± 1.134) | |
| End of study (n=83, 28, 55) | 5.829 (± 1.1434) | 5.956 (± 0.9431) | 5.765 (± 1.2361) | |
| Endpoint (n=1030, 472, 558) | 5.587 (± 1.1503) | 5.535 (± 1.169) | 5.631 (± 1.1334) | |

Notes:

[34] - Safety analysis set of participants with assessments at stated timeframes

[35] - Safety analysis set of participants with assessments at stated timeframes

[36] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With a Positive Anti-Reslizumab Antibody Status at Baseline, Weeks 24, 48, 72, 96, End of Study, Endpoint and Overall

| | |
|-----------------|--|
| End point title | Participants With a Positive Anti-Reslizumab Antibody Status at Baseline, Weeks 24, 48, 72, 96, End of Study, Endpoint and Overall |
|-----------------|--|

End point description:

Blood samples were collected for the determination of anti-drug antibody (ADAs) before study drug infusion at baseline and every 24 weeks until end of treatment visit or early withdrawal. Serum samples were analyzed by Teva (Teva Biopharmaceuticals USA, Rockville, Maryland, USA) using a validated homogeneous solution based bridging enzyme linked immune sorbent assay (Mikulsis et al 2011, Qui et al 2010). The analysis of anti-reslizumab antibody in patient serum consists of 3 tiers of assays for screening, confirmation, and titer analysis. If a participant had a treatment-emergent ADA response (ie, ADA positive at any of the postdose time points but negative at the predose time point) or if there was a treatment-boosted ADA response (defined as a greater than 4-fold increase from a positive baseline ADA response (Shankar et al 2014), the participant was classified as overall ADA positive.

Predose samples for the reslizumab-experienced participants came from the previous studies.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 24, 48, 72, 96, End of Study, Endpoint and Overall

| End point values | Previous Placebo-Treated Subpopulation | Previous Reslizumab-Treated Subpopulation | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 480 ^[37] | 571 ^[38] | | |
| Units: participants | | | | |
| Overall (n=466, 548) | 24 | 25 | | |
| Baseline (n=442, 541) | 16 | 24 | | |
| Week 24 (n=382, 445) | 12 | 13 | | |
| Week 48 (n=187, 247) | 9 | 7 | | |
| Week 72 (n=56, 104) | 4 | 4 | | |
| Week 96 (n=24, 48) | 3 | 1 | | |
| End of study (n=142, 52) | 4 | 1 | | |
| Endpoint (n=466, 545) | 12 | 17 | | |

Notes:

[37] - Safety analysis set of participants with assessments at stated timeframes

[38] - Safety analysis set of participants with assessments at stated timeframes

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (post-dose) to Week 65. The endpoint for adverse events was the last post-baseline observation, which included the 90 day follow-up visit.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Reslizumab 3.0 mg/kg |
|-----------------------|----------------------|

Reporting group description:

Reslizumab 3.0 mg/kg administered intravenously once every 4 weeks (+-7 days) for up to 24 months.

| Serious adverse events | Reslizumab 3.0 mg/kg | | |
|---|----------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 78 / 1051 (7.42%) | | |
| number of deaths (all causes) | 3 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 3 / 1051 (0.29%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ovarian epithelial cancer | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|------------------|--|--|
| Metastases to lung | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphoma | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Borderline ovarian tumour | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal cancer | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vascular disorders | | | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Suprapubic pain | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-------------------|--|--|
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hernia | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Endometrial hyperplasia | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 18 / 1051 (1.71%) | | |
| occurrences causally related to treatment / all | 3 / 24 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nasal polyps | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pleural effusion | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nasal septum deviation | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Asthmatic crisis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aggression | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Liver function tests abnormal | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural | | | |

| | | | |
|---|------------------|--|--|
| complications | | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skull fractured base | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|------------------|--|--|
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |

| | | | |
|---|------------------|--|--|
| Transient ischaemic attack subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorder subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Carpal tunnel syndrome subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders Amaurosis fugax subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders Pneumoperitoneum subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Umbilical hernia subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Megacolon subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|------------------|--|--|
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Drug eruption | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Urethral stenosis | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stress urinary incontinence | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 1051 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|------------------|--|--|--|
| Peritonitis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mastoiditis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of bronchiectasis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis pneumococcal | | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious pleural effusion | | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 1051 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Reslizumab 3.0 mg/kg | | |
|---|----------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 519 / 1051 (49.38%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 73 / 1051 (6.95%) | | |
| occurrences (all) | 106 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 301 / 1051 (28.64%) | | |
| occurrences (all) | 563 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 107 / 1051 (10.18%) | | |
| occurrences (all) | 141 | | |

| | | | |
|-----------------------------|------------------------|--|--|
| Nasopharyngitis | | | |
| subjects affected / exposed | 150 / 1051 (14.27%) | | |
| occurrences (all) | 226 | | |
| Sinusitis | | | |
| subjects affected / exposed | 77 / 1051 (7.33%) | | |
| occurrences (all) | 114 | | |
| Bronchitis | | | |
| subjects affected / exposed | 62 / 1051 (5.90%) | | |
| occurrences (all) | 77 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 04 February 2011 | <p>The following major changes (not all inclusive) were made to the protocol:</p> <ul style="list-style-type: none">• the original title of the protocol "A 24 Month Open Label Extension Study to Evaluate the Long Term Safety and Efficacy of Reslizumab (3.0 mg/kg) as Treatment for Patients (12 Through 75 Years of Age) With Eosinophilic Asthma Who Completed a Prior Cephalon Sponsored Study in Eosinophilic Asthma" was changed, because study treatment could be as long as 104 weeks (26 months) and the age range was already specified in the protocol• clinical laboratory tests were added at weeks 4 and 8, and all objectives and endpoints relative to these measures were revised to include the data collected• text was revised to clarify that the reslizumab dose is based on baseline body weight• footnote "o" was added for vital signs measurements at visit 1• text regarding informed consent for minors was revised to reflect that only 1 parent was required to sign the informed consent form• the word "rescue" was deleted when used regarding SABA use review• the administration rate for reslizumab was corrected from 2 mg/min to 2 mL/min• text was revised to clarify that the investigator may adjust the dose for concomitant medications taken for asthma based on best clinical practices• the time for refraining from SABA use before study visits was changed from 4 to 6 hours• text regarding monitoring of adverse events during any washout phase of the study was deleted since this open label study did not have a washout phase• text regarding safety variables and analysis was revised to reflect additional analysis of clinical laboratory test results at weeks 4 and 8 |
| 14 April 2011 | <p>The following major changes (not all inclusive) were made to the protocol:</p> <ul style="list-style-type: none">• administrative changes were documented• a 90 day follow up evaluation was added for the assessment of adverse events, blood eosinophils, and vital signs to allow for additional safety monitoring• in addition to standard safety monitoring by the sponsor, an independent DSMB was implemented to oversee the safety of the patients |
| 19 April 2011 | <p>The following major changes (not all inclusive) were made to the protocol:</p> <ul style="list-style-type: none">• a change was made to stipulate that blood samples were to be collected for pharmacokinetic evaluation, blood eosinophil determination, and anti reslizumab antibody assessment each time a patient experienced a serious adverse event, an adverse event leading to withdrawal, or an exacerbation of asthma symptoms• inclusion criteria (a) and (b) were changed for clarification of country specific age requirements• exclusion criterion (f) was revised to clarify acceptable contraceptive methods to be used during the study |

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|---------------|---|
| 19 April 2013 | <p>Amendment 4 (dated 19 April 2013) to the protocol was issued after 627 patients were enrolled into the study. Changes to the protocol were considered to have no negative impact on the safety of patients already enrolled into the study.</p> <p>The following major changes (not all inclusive) were made to the protocol:</p> <ul style="list-style-type: none"> • Cephalon was acquired and became an affiliate of Teva Branded Pharmaceutical Products R&D, Inc; administrative changes due to the acquisition were reflected, where appropriate, in the study protocol • clinical laboratory information was revised to encompass appropriate countries • background information was clarified/restated and a table with completed clinical studies of reslizumab was added for harmonization with other reslizumab study protocols • pharmacokinetic, pharmacodynamic, and immunogenicity content was added for clarification • patient population with eosinophilic asthma qualified as "moderate to severe" • added to 90 day follow up evaluation: (± 7 days) • immunogenicity (from anti reslizumab antibody assessment) was removed as a safety evaluation in the study • text for emergency treatment was added to include: unscheduled visits to the physician's office for nebulizer treatment or other urgent treatment to prevent worsening of asthma symptoms, or a visit to the emergency room for treatment, regardless of subsequent admission • beta agonist use was qualified as "short acting" and % FEV1 as % "predicted" • text was added to specify who was required to have a urine β HCG test • IRT registration was added to the procedure and assessment schedule • baseline body weight was specified to be used throughout the study to determine dose |
| 14 April 2014 | <p>Teva communicated its intent to terminate Study C38072/3085 to all investigators involved with the trial on 09 January 2014. The rationale for the termination was that the primary study objective, in terms of open label events for patient exposure to an investigational product without confirmed benefit/risk, had been sufficiently met. This was primarily based on substantial over-enrollment from the originally planned sample size (approximately 740 patients) and is consistent with the Stopping Rules and Discontinuation Criteria in Section 3.6 of the original protocol. The decision to terminate the study was not due to any new or emerging safety concerns at that time. Following study termination, protocol amendment 5 was developed and issued on 14 April 2014 in countries within the European Union to comply with applicable EU legislation in this particular circumstance. This revised protocol was submitted and approved in all EU countries.</p> <p>The following major procedural changes (not all inclusive) were made to the protocol:</p> <ul style="list-style-type: none"> • change in signatory and administration of the study • purpose of the study was redefined to align with changes to the primary objective, ie, obtaining additional safety data for reslizumab • planned enrollment increased from 740 to 1000 patients, as actual enrollment exceeded initial predictions • decision to terminate the study early (duration "up to 24 months") as exposure to study drug had been met with no new or emerging safety or efficacy concerns • duration of patient participation was corrected to include 90 day follow up visit • study was defined as being complete when the last patient completed his/her last study visit |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported