



Clinical trial results:

A randomized, open label, parallel-group, international, multicenter study evaluating persistency of response to omalizumab during 32 weeks treatment given as add on to optimized asthma therapy in adult and adolescent patients with severe allergic asthma, who remain inadequately controlled despite GINA (2004) Step 4 therapy

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2005-001099-11 |
| Trial protocol | GB NO IE ES DK SE DE HU PT IT BE GR |
| Global end of trial date | 23 September 2008 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 13 July 2016 |
| First version publication date | 15 August 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CIGE025A2425 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00264849 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |

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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 23 September 2008 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 September 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate persistency in treatment responder classification between assessments at 16 and 32 weeks after starting omalizumab therapy given as add on to optimized asthma therapy in patients who remained uncontrolled despite GINA (2004) Step 4 therapy. Treatment response was defined by at least marked improvement of overall asthma control as assessed by physician Global Evaluation of Treatment Effectiveness.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial. The subjects were treated with β -2 agonist (salbutamol or terbutaline) for rescue medication from symptoms of intercurrent bronchospasm or during asthma exacerbation, inhaled via any device e.g. MDI Accuhaler, Rotacaps, Turbuhaler and Ventidisks. If rescue medication was taken prior to a spirometric assessment, the investigator was notified by the subject. Home use of nebulized β -2 agonist (salbutamol 2.5-5 milligram (mg) or terbutaline 5-10 mg) was allowed for treatment. Symptomatic subjects despite nebulization contacted trial personnel immediately for further evaluation, each nebulization was recorded on subject's diary/note book.

Background therapy:

Subjects were receiving any of the following background therapies (Oral and/or inhaled corticosteroids (ICS), Long-acting inhaled β -2 agonists (LABA), Fixed dose combinations of ICS and LABA) at least 3 months prior to screening with doses adjusted according to best clinical practice during the 32 weeks treatment:

1. Oral and ICS: Subjects inhaled moderate to high dose of corticosteroids more than or equal to (\geq)800 microgram (mcg) beclomethasone dipropionate (BDP) or equivalent prior to the 2 qualifying asthma exacerbations, required treatment with systemic corticosteroids for at least 3 months prior to screening. Doses of ICS more than ($>$)1000 mcg BDP or equivalent, were taken for at least the last 4 weeks of the run-in period.
2. LABA: Subjects were to have taken LABA at least 3 months prior to screening and remain on unchanged dose during the last 4 weeks of run-in. Subjects were not allowed LABA medication within 12 hours prior to visit for reversibility and spirometric assessment.
3. Fixed dose combinations of ICS and LABA: Subjects were allowed with fixed combination (budesonide/formoterol or fluticasone/salmeterol) with a dose of ICS \geq 800 mcg BDP or equivalent. Doses of inhaled corticosteroid (ICS) more than ($>$)1000 mcg BDP or equivalent, were taken for at least the last 4 weeks of the run-in period. Fixed dose combination medication should have been taken after spirometry measurements. Additional medications for treatment of the patient's allergic asthma exacerbations already established prior to the final 4 weeks of the run in period were allowed in this study

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 22 November 2005 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Spain: 39 |
| Country: Number of subjects enrolled | Sweden: 8 |
| Country: Number of subjects enrolled | United Kingdom: 36 |
| Country: Number of subjects enrolled | Belgium: 21 |
| Country: Number of subjects enrolled | Denmark: 9 |
| Country: Number of subjects enrolled | Germany: 48 |
| Country: Number of subjects enrolled | Hungary: 30 |
| Country: Number of subjects enrolled | Italy: 99 |
| Country: Number of subjects enrolled | Canada: 15 |
| Country: Number of subjects enrolled | Israel: 16 |
| Country: Number of subjects enrolled | Poland: 40 |
| Country: Number of subjects enrolled | Switzerland: 3 |
| Country: Number of subjects enrolled | Turkey: 35 |
| Worldwide total number of subjects | 400 |
| EEA total number of subjects | 331 |

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) | 5 |
| Adults (18-64 years) | 368 |
| From 65 to 84 years | 27 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 106 centres in 14 countries.

Pre-assignment

Screening details:

A total of 768 subjects were screened, out of which 406 were provided with treatment. Out of 406 treated subjects, 2 subjects treated with optimized asthma treatment (OAT) + omalizumab were non-randomised and discontinued due to administrative problems.

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 404 ^[1] |
| Number of subjects completed | 400 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Consent withdrawn by subject: 2 |
| Reason: Number of subjects | Protocol deviation: 1 |
| Reason: Number of subjects | lost to follow up: 1 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 406 treated subjects, 2 subjects treated with optimized asthma treatment (OAT) + omalizumab were nonrandomised and discontinued due to administrative problems.

Period 1

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

Blinding implementation details:

The study was open label, hence no blinding was performed.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---|
| Arm title | Optimized Asthma Treatment (OAT) + Omalizumab |
|------------------|---|

Arm description:

Subjects received omalizuamab (150 mg; 225 mg; 300 mg or 375 mg) through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels.

Subjects with body- weight between 90-150 kilograms (kg), received 300 mg of omalizumab for omalizumab for 4 weeks (if pre-treatment IgE

level was between 30-100 international units per milliliter [IU/mL]) and for 2 weeks (if pre-treatment Ig E level was between 200-300 IU/mL).

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Omalizumab |
| Investigational medicinal product code | IGE025 |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Omalizumab 150 mg administered s.c. after reconstitution with 1.4 ml Sterile Water for Injection. The dose administered was individualized for each subject based on the body weight.

| | |
|------------------|----------------------------------|
| Arm title | Optimized Asthma Treatment (OAT) |
|------------------|----------------------------------|

Arm description:

During the 32 weeks treatment phase , subjects continued to receive OAT were evaluated and optimized according to GINA guidelines established during the run-in period of the study. The subjects were treated with moderate to high dose ICS (BDP 1000 mcg or equivalent dose), regular LABA, or fixed combination of ICS and LABA.

| | |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

| Number of subjects in period 1 | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) |
|---------------------------------------|---|----------------------------------|
| Started | 272 | 128 |
| Completed | 253 | 106 |
| Not completed | 19 | 22 |
| Adverse event, serious fatal | - | 1 |
| Consent withdrawn by subject | 7 | 9 |
| Adverse event, non-fatal | 7 | 2 |
| Unsatisfactory therapeutic effect | 1 | 6 |
| Lost to follow-up | - | 1 |
| Protocol deviation | 4 | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Optimized Asthma Treatment (OAT) + Omalizumab |
|-----------------------|---|

Reporting group description:

Subjects received omalizumab (150 mg; 225 mg; 300 mg or 375 mg) through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Subjects with body- weight between 90-150 kilograms (kg), received 300 mg of omalizumab for 4 weeks (if pre-treatment IgE level was between 30-100 international units per milliliter [IU/mL]) and for 2 weeks (if pre-treatment IgE level was between 200-300 IU/mL).

| | |
|-----------------------|----------------------------------|
| Reporting group title | Optimized Asthma Treatment (OAT) |
|-----------------------|----------------------------------|

Reporting group description:

During the 32 weeks treatment phase , subjects continued to receive OAT were evaluated and optimized according to GINA guidelines established during the run-in period of the study. The subjects were treated with moderate to high dose ICS (BDP 1000 mcg or equivalent dose), regular LABA, or fixed combination of ICS and LABA.

| Reporting group values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | Total |
|---------------------------------------|---|----------------------------------|-------|
| Number of subjects | 272 | 128 | 400 |
| Age categorical Units: Subjects | | | |
| 12-17 years | 5 | 0 | 5 |
| 18-54 years | 189 | 92 | 281 |
| 55-64 years | 61 | 26 | 87 |
| 65-75 years | 17 | 10 | 27 |
| Age continuous | | | |
| Mod ITT | | | |
| Units: years | | | |
| arithmetic mean | 45.6 | 45.7 | |
| standard deviation | ± 13.04 | ± 12.57 | - |
| Gender categorical Units: Subjects | | | |
| Female | 183 | 76 | 259 |
| Male | 89 | 52 | 141 |

End points

End points reporting groups

| | |
|-----------------------|---|
| Reporting group title | Optimized Asthma Treatment (OAT) + Omalizumab |
|-----------------------|---|

Reporting group description:

Subjects received omalizumab (150 mg; 225 mg; 300 mg or 375 mg) through subcutaneous (s.c) route for 2-4 weeks based on their body weight and immunoglobulin E (IgE) levels. Subjects with body- weight between 90-150 kilograms (kg), received 300 mg of omalizumab for 4 weeks (if pre-treatment IgE level was between 30-100 international units per milliliter [IU/mL]) and for 2 weeks (if pre-treatment IgE level was between 200-300 IU/mL).

| | |
|-----------------------|----------------------------------|
| Reporting group title | Optimized Asthma Treatment (OAT) |
|-----------------------|----------------------------------|

Reporting group description:

During the 32 weeks treatment phase , subjects continued to receive OAT were evaluated and optimized according to GINA guidelines established during the run-in period of the study. The subjects were treated with moderate to high dose ICS (BDP 1000 mcg or equivalent dose), regular LABA, or fixed combination of ICS and LABA.

Primary: Persistency rate of response and non-response, as based on investigator's Global Evaluation of Treatment Effectiveness

| | |
|-----------------|---|
| End point title | Persistency rate of response and non-response, as based on investigator's Global Evaluation of Treatment Effectiveness ^[1] |
|-----------------|---|

End point description:

Treatment response of omalizumab was assessed by investigator based on GETE, a five point scale that evaluated change in asthma control/symptoms (1: excellent for complete control of asthma, 2: good for marked improvement of asthma, 3: moderate for discernible, but limited improvement of asthma, 4: poor for no appreciable change, and 5: worsening of asthma). Responders were defined as subjects scaling excellent or good and non-responders as moderate, poor or worsening assessed at 16 weeks and 32 weeks. The primary analysis was performed in the modified intent to treat (ITT) population, defined as all randomized subjects with at least one post-baseline efficacy assessment. Here, "Number of subjects analysed" were subjects assessed for persistency of response if they were responders at Week 16 and had a second GETE obtained ≥ 4 weeks after the Week 16 assessment or discontinued prematurely for unsatisfactory therapeutic effect ≥ 4 weeks after the Week 16 assessment.

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

End point timeframe:

Week 16, Week 32

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: The statistics for this end point was planned for selected arm only.

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|----------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 187 | 28 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 91.4 (87.4 to 95.5) | 64.3 (46.5 to 82) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects by Investigator's Global Evaluation of Treatment Effectiveness (GETE) category at Week 16 and Week 32

| | |
|-----------------|--|
| End point title | Number of subjects by Investigator's Global Evaluation of Treatment Effectiveness (GETE) category at Week 16 and Week 32 |
|-----------------|--|

End point description:

Responders were defined as subjects scaling excellent or good at 16 weeks and still at 32 weeks. Response for subjects were assessed by investigator based on completion of a GETE, which was a five point scale that evaluates change in asthma control/symptoms (excellent for complete control of asthma, good for marked improvement of asthma, moderate for discernible, but limited improvement of asthma, poor for no appreciable change, and worsening for asthma). The analysis was performed in the modified ITT population.

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

End point timeframe:

Week 16, Week 32

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|-----------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Number of subjects | | | | |
| Week 16: Excellent | 35 | 1 | | |
| Week 16: Good | 155 | 28 | | |
| Week 16: Moderate | 57 | 24 | | |
| Week 16: Poor | 13 | 34 | | |
| Week 16: Worsening | 1 | 6 | | |
| Week 16: Missing | 11 | 35 | | |
| Week 32: Excellent | 73 | 1 | | |
| Week 32: Good | 126 | 24 | | |
| Week 32: Moderate | 45 | 31 | | |
| Week 32: Poor | 13 | 39 | | |
| Week 32: Worsening | 2 | 9 | | |
| Week 32: Missing | 13 | 24 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects by Subject's Global Evaluation of Treatment Effectiveness (GETE) category at Week 16 and Week 32

| | |
|-----------------|---|
| End point title | Number of subjects by Subject's Global Evaluation of Treatment Effectiveness (GETE) category at Week 16 and Week 32 |
|-----------------|---|

End point description:

Responders were defined as subjects scaling excellent or good at 16 weeks and still at 32 weeks. Response for subjects were evaluated by subjects based on completion of a GETE, which was a five point scale that evaluates change in asthma control/symptoms (excellent for complete control of asthma, good for marked improvement of asthma, moderate for discernible, but limited improvement of asthma, poor for no appreciable change, and worsening for asthma). The analysis was performed in the modified ITT population.

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

End point timeframe:

Week 16, Week 32

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|-----------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Number of subjects | | | | |
| Week 16: Excellent | 54 | 4 | | |
| Week 16: Good | 139 | 29 | | |
| Week 16: Moderate | 53 | 23 | | |
| Week 16: Poor | 15 | 33 | | |
| Week 16: Worsening | 1 | 5 | | |
| Week 16: Missing | 10 | 34 | | |
| Week 32: Excellent | 80 | 2 | | |
| Week 32: Good | 127 | 27 | | |
| Week 32: Moderate | 38 | 28 | | |
| Week 32: Poor | 12 | 38 | | |
| Week 32: Worsening | 2 | 8 | | |
| Week 32: Missing | 13 | 25 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of persistent treatment non-responders based on Investigator's Global Evaluation of Treatment Effectiveness (GETE) score at both Week 16 and Week 32

| | |
|-----------------|---|
| End point title | Percentage of persistent treatment non-responders based on Investigator's Global Evaluation of Treatment Effectiveness (GETE) score at both Week 16 and Week 32 |
|-----------------|---|

End point description:

Treatment response was assessed by investigator based on GETE, a five point scale that evaluated change in asthma control/symptoms (1: excellent for complete control of asthma, 2: good for marked improvement of asthma, 3: moderate for discernible, but limited improvement of asthma, 4: poor for no appreciable change, and 5: worsening for asthma). Non-responders were defined as moderate, poor or worsening assessed at 16 weeks and 32 weeks. The analysis was performed in the modified ITT population. Here, "Number of subjects analysed" were subjects assessed for persistency of non-response if they were non-responders at Week 16 and had second GETE obtained ≥ 4 weeks after the week 16 assessment or discontinued prematurely for unsatisfactory therapeutic effect ≥ 4 weeks after the week 16 assessment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 16, Week 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|----------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 63 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 62 (50.7 to 73.3) | 90.5 (83.2 to 97.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Predicted Forced Expiratory Volume for 1 Second (FEV1)

| | |
|-----------------|--|
| End point title | Percent Predicted Forced Expiratory Volume for 1 Second (FEV1) |
|-----------------|--|

End point description:

FEV1 was defined as the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. The subject's predicted FEV1 value was calculated according to Crapo standards (Males: Predicted FEV1 = 0.0414*height – 0.0244*age – 2.190 and Females: Predicted FEV1 = 0.0342*height – 0.0255*age – 1.578, where height was in cm). The analysis was performed in modified ITT population. Here, 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Weeks 16, Week 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|--|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Percent predicted FEV1 | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 16 (n= 258, 106) | 68.4 (66.2 to 70.5) | 64.8 (61.8 to 67.8) | | |
| Week 32 (n= 266, 121) | 68.1 (65.8 to 70.5) | 63.7 (60.6 to 66.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire (ACQ) overall score at Week 16 and Week 32

| | |
|-----------------|---|
| End point title | Change from baseline in Asthma Control Questionnaire (ACQ) overall score at Week 16 and Week 32 |
|-----------------|---|

End point description:

Asthma Control Questionnaire (ACQ), has 7 questions, each with a 7 point scale (0 – good control, 6 – poor control). The average score will be calculated as the total of all 7 questions divided by 7 (or the number of questions that were answered at the time point as long as there are at least 4 questions answered). A negative change in score indicated improvement in symptoms. The analysis was performed in modified ITT population. Here 'n' signifies those subjects with valid ACQ measurements at specified time points for each group, respectively.

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

End point timeframe:

Baseline, Weeks 16, Week 32

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|--|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Units on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 16 (n= 249, 104) | -0.78 (-0.92 to -0.63) | -0.11 (-0.31 to 0.1) | | |
| Week 32 (n= 238, 104) | -0.91 (-1.07 to -0.76) | -0.04 (-0.26 to 0.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with clinically significant asthma exacerbations during the 32 week treatment period

| | |
|-----------------|---|
| End point title | Percentage of subjects with clinically significant asthma exacerbations during the 32 week treatment period |
|-----------------|---|

End point description:

A clinically significant asthma exacerbation was defined as a worsening of asthma requiring treatment with rescue systemic (oral or IV) corticosteroids. The initiation of the rescue systemic corticosteroids

was marked as the start of asthma exacerbation and cessation of the rescue systemic corticosteroids was marked as the end. Duplicated, or overlapped by at least one day with another episode, or nested within another exacerbation episode, were considered as single exacerbation. The analysis was performed in the modified ITT population.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Weeks 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|-------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0 asthma exacerbation | 67.3 | 50 | | |
| 1 asthma exacerbation | 21.3 | 27.3 | | |
| 2 asthma exacerbation | 6.6 | 13.3 | | |
| 3 asthma exacerbation | 3.3 | 4.7 | | |
| >= 4 asthma exacerbation | 1.5 | 4.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with severe asthma exacerbations during the 32 week treatment period

| | |
|--|---|
| End point title | Percentage of subjects with severe asthma exacerbations during the 32 week treatment period |
| End point description: | |
| Subjects with clinically significant severe asthma exacerbation fulfilled any of the following criteria: required treatment with rescue systemic (oral or IV) corticosteroids, or resulted in hospitalization or required an emergency department visit, or resulted in >30% fall from personal best in peak expiratory flow for two successive days. The analysis was performed in the modified ITT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Week 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|-------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Percentage of subjects | | | | |

| | | | | |
|----------------------------------|------|------|--|--|
| number (not applicable) | | | | |
| 0 asthma exacerbations severe | 84.6 | 77.3 | | |
| 1 asthma exacerbations severe | 11.8 | 13.3 | | |
| 2 asthma exacerbations severe | 1.8 | 5.5 | | |
| 3 asthma exacerbations severe | 0.7 | 1.6 | | |
| >= 4 asthma exacerbations severe | 1.1 | 2.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hospital admissions, emergency room visits and unscheduled clinical visits due to asthma exacerbations

| | |
|-----------------|--|
| End point title | Percentage of subjects with hospital admissions, emergency room visits and unscheduled clinical visits due to asthma exacerbations |
|-----------------|--|

End point description:

Combined total of unscheduled visits was determined for each subject as the total number of hospital admissions, emergency room visits and unscheduled outpatient clinical visits due to asthma exacerbations. Only the most serious type of asthma exacerbation was included for multiple type of visit on same day, while all visits were counted when visits occurred on different dates for single asthma exacerbation. The analysis was performed in the modified ITT population.

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

End point timeframe:

Day 1 up to Week 32

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|----------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0 combined unscheduled visits | 83.1 | 67.2 | | |
| 1 combined unscheduled visits | 9.6 | 9.4 | | |
| 2 combined unscheduled visits | 3.7 | 13.3 | | |
| 3 combined unscheduled visits | 1.5 | 6.3 | | |
| >= 4 combined unscheduled visits | 2.2 | 3.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in oral steroid dose at Weeks 16 and Week 32

| | |
|---|--|
| End point title | Percentage change from baseline in oral steroid dose at Weeks 16 and Week 32 |
| End point description: The dose of oral steroid measured was the maintenance dose of the subjects and not the dose to treat an asthma exacerbation. A negative change from baseline indicated improvement. The analysis was performed in the modified ITT population. Here, "Number of subjects analysed" were subjects evaluable for change from baseline in oral steroid dose at week 16 and week 32, for each arm. The 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 16, Week 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|---------------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 23 | | |
| Units: Prednisolone equivalent mg/day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 16 (n= 56, 19) | -20.1 (± 63.08) | 36.8 (± 212.03) | | |
| Week 32 (n= 59, 23) | -45 (± 50.22) | 18.3 (± 85.13) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects by type of dose change for systemic steroids at Weeks 16 and Week 32

| | |
|--|---|
| End point title | Percentage of subjects by type of dose change for systemic steroids at Weeks 16 and Week 32 |
| End point description: Subjects with systemic steroids were defined as those who used systemic steroids throughout the entire treatment period (Weeks 16 and Week 32). Dose of systemic steroids was expressed in prednisolone equivalent mg/day. Removed subjects were defined as subjects who removed from systemic steroids during treatment period and not provided with dose, maintained as subjects with unchanged or increased dose and decreased as subjects with decreased dose. The analysis was performed in the modified ITT population. Here, "Number of subjects analysed" were subjects evaluable for change from baseline in oral steroid dose at week 16 and week 32, for each arm. The 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 16, Week 32 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|---|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 23 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 16 - Removed systemic steroids (n= 56, 19) | 17.9 | 10.5 | | |
| Week 32 - Removed systemic steroids (n= 59, 23) | 32.2 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Quality of Life Questionnaire (AQLQ) overall score at Week 15 and Week 31

| | |
|-----------------|--|
| End point title | Change from baseline in Asthma Quality of Life Questionnaire (AQLQ) overall score at Week 15 and Week 31 |
|-----------------|--|

End point description:

Asthma Quality of Life Questionnaire (AQLQ) was 32 item questionnaire defined in 4 domains (symptoms, activity limitation, emotional function and environmental exposure). Each question was answered on a 7 point scale (1–totally limited/problems all the time to 7–not at all limited/no problems). The overall AQLQ score was the mean of all 32 responses (a minimum domain / overall score of 1 = Severely impaired whereas a maximum domain / overall score of 7 = not impaired at all). A positive change from baseline score indicated improvement. The analysis was performed in the modified ITT population. The 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

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

End point timeframe:

Baseline, Week 15, Week 31

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|--|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Units on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Overall Score: Week 15 (n= 214, 92) | 0.9 (0.73 to 1.07) | 0.03 (-0.2 to 0.27) | | |
| Overall Score: Week 31 (n= 224, 97) | 1.06 (0.88 to 1.24) | -0.07 (-0.31 to 0.17) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in EuroQual 5-Dimension health status questionnaire (EQ-5D) utility index and health state assessment at Week 15 and Week 31

| | |
|-----------------|---|
| End point title | Change from baseline in EuroQual 5-Dimension health status questionnaire (EQ-5D) utility index and health state assessment at Week 15 and Week 31 |
|-----------------|---|

End point description:

The utility-based EQ-5D questionnaire was in two parts and provides a generic measure of health for clinical and economic appraisal. The health state classification part contains 5 questions each with 3 categories (no problem, moderate problem, severe problems). The visual analogue scale was measured from 0 (worst imaginable health state) to 100 (best imaginable health state). A positive change from baseline score indicated improvement. The analysis was performed in the modified ITT population. Here 'n' signifies those subjects evaluable for this measure at specified time points for each group, respectively.

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

End point timeframe:

Baseline, Week 15, Week 31

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|---|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 272 | 128 | | |
| Units: Units on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| EQ-5D Utility Index Score: Week 15 (n= 212 ,90) | 0.071 (0.038 to 0.105) | 0.002 (-0.044 to 0.049) | | |
| EQ-5D Utility Index Score: Week 31 (n= 194, 81) | 0.091 (0.051 to 0.132) | 0.064 (0.008 to 0.121) | | |
| Health State Assessment: Week 15 (n= 211, 89) | 8.2 (4.7 to 11.8) | -0.4 (-5.4 to 4.6) | | |
| Health State Assessment: Week 31 (n= 194, 80) | 9.3 (5.2 to 13.4) | -2.8 (-8.5 to 3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in percent overall Work Impairment due to asthma symptoms at Week 31

| | |
|-----------------|---|
| End point title | Change from baseline in percent overall Work Impairment due to asthma symptoms at Week 31 |
|-----------------|---|

End point description:

Work Productivity and Activity Impairment-Allergic Asthma (WPAI-AA) questionnaire, covered 6 questions relating to hours missed from work and work productivity in the previous 7 days. Overall work impairment due to asthma problems was derived from the proportion of hours missed from work due to

asthma and the degree to which asthma problems affected productivity while working. A negative change indicated improvement. The analysis was performed in the modified ITT population. Here, "Number of subjects analysed" were subjects evaluable for this measure at specified time points for each group, respectively.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 31 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|--------------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 79 | 34 | | |
| Units: Percent impairment | | | | |
| arithmetic mean (standard deviation) | -21.4 (\pm 26.79) | 0 (\pm 29.89) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in percent Activity Impairment due to asthma symptoms at Week 31

| | |
|-----------------|---|
| End point title | Change from baseline in percent Activity Impairment due to asthma symptoms at Week 31 |
|-----------------|---|

End point description:

Work Productivity and Activity Impairment-Allergic Asthma (WPAI-AA) questionnaire, covered 6 questions relating to hours missed from work and work productivity in the previous 7 days. Activity impairment due to asthma problems was derived from the subjects assessment of the degree to which asthma problems affected regular activities. A negative change indicated improvement. The analysis was performed in the modified ITT population. Here, "Number of subjects analysed" were subjects evaluable for this measure at specified time points for each group, respectively.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 31 | |

| End point values | Optimized Asthma Treatment (OAT) + Omalizumab | Optimized Asthma Treatment (OAT) | | |
|--------------------------------------|---|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 193 | 80 | | |
| Units: Percent impairment | | | | |
| arithmetic mean (standard deviation) | -17.2 (\pm 24.36) | -0.1 (\pm 24.05) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Optimized Asthma Treatment |
|-----------------------|----------------------------|

Reporting group description:

Optimized Asthma Treatment

| | |
|-----------------------|---|
| Reporting group title | Optimized Asthma Treatment + Omalizumab |
|-----------------------|---|

Reporting group description:

Optimized Asthma Treatment + Omalizumab

| Serious adverse events | Optimized Asthma Treatment | Optimized Asthma Treatment + Omalizumab | |
|---|----------------------------|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 128 (13.28%) | 29 / 274 (10.58%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast neoplasm | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Haematoma | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Intra-uterine death | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| 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 | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyp | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 14 / 128 (10.94%) | 15 / 274 (5.47%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status asthmaticus | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Chest injury | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 2 / 274 (0.73%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 2 / 274 (0.73%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fractured coccyx | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 3 / 274 (1.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| 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 | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Melaena | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperparathyroidism | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| 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 | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 274 (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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 128 (1.56%) | 0 / 274 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Lower respiratory tract infection subjects affected / exposed | 1 / 128 (0.78%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed | 0 / 128 (0.00%) | 1 / 274 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Optimized Asthma Treatment | Optimized Asthma Treatment + Omalizumab | |
|---|-----------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 66 / 128 (51.56%) | 151 / 274 (55.11%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 128 (7.03%) | 33 / 274 (12.04%) | |
| occurrences (all) | 26 | 92 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 51 / 128 (39.84%) | 82 / 274 (29.93%) | |
| occurrences (all) | 52 | 85 | |
| Cough | | | |
| subjects affected / exposed | 4 / 128 (3.13%) | 14 / 274 (5.11%) | |
| occurrences (all) | 6 | 19 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 14 / 274 (5.11%) | |
| occurrences (all) | 1 | 15 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 14 / 274 (5.11%) | |
| occurrences (all) | 0 | 19 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 7 / 128 (5.47%) | 13 / 274 (4.74%) | |
| occurrences (all) | 10 | 14 | |
| Influenza | | | |
| subjects affected / exposed | 4 / 128 (3.13%) | 18 / 274 (6.57%) | |
| occurrences (all) | 4 | 22 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 128 (7.03%) | 38 / 274 (13.87%) | |
| occurrences (all) | 14 | 52 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 8 / 128 (6.25%) | 16 / 274 (5.84%) | |
| occurrences (all) | 14 | 20 | |
| Upper respiratory tract infection | | | |

| | | | |
|-----------------------------|-----------------|------------------|--|
| subjects affected / exposed | 6 / 128 (4.69%) | 17 / 274 (6.20%) | |
| occurrences (all) | 7 | 20 | |
| Sinusitis | | | |
| subjects affected / exposed | 7 / 128 (5.47%) | 10 / 274 (3.65%) | |
| occurrences (all) | 12 | 18 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 23 June 2006 | <ul style="list-style-type: none">• The secondary objective to further evaluate the best individual or combination of clinical measures for evaluating treatment response to omalizumab treatment was introduced• The dose of omalizumab to be given every 4-weeks for a body weight >30-40 and baseline IgE >200-300 international units per millilitre(IU/ml) to 225 mg, was introduced to be consistent with the approved dosing schedule• Total IgE measurement at randomisation visit was added |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported