



## Clinical trial results:

### A 24 Week, Open Label, Multi-center Evaluation of Pharmacokinetics and Pharmacodynamics, Efficacy and Safety of Omalizumab in Japanese Children (6 - 15 Years) With Inadequately Controlled Allergic Asthma Despite Current Recommended Treatment

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-003534-27   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 17 February 2012 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 04 January 2017 |
| First version publication date | 04 January 2017 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CIGE025B1301 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01155700 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharmaceuticals AG   |
| Sponsor organisation address | CH-4002, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111, |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharmaceuticals 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? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 17 February 2012 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 17 February 2012 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To examine whether the geometric mean of serum free IgE level at 24 weeks of the treatment period in Japanese pediatric patients reaches under 25 ng/mL (target level).

Protection of trial subjects:

Patients were permitted to use any rescue medication for asthma attacks/exacerbations on an as needed (prn) basis during the treatment period.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 18 June 2010 |
| 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 | Japan: 38 |
| Worldwide total number of subjects   | 38        |
| EEA total number of subjects         | 0         |

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)                     | 21 |
| Adolescents (12-17 years)                 | 17 |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 38 patients were treated and completed the study therefore no patients discontinued the study.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Omalizumab |
|------------------|------------|

Arm description:

Omalizumab treatment

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

Dosage and administration details:

Omalizumab 75 to 375 mg was administered subcutaneously every 2 or 4 weeks. Doses (mg) and dosing frequency were determined from dosing tables based on the patient' serum total IgE level (IU/mL) and body weight (kg) measured at Visit 1 (run-in period).

|                                       |            |
|---------------------------------------|------------|
| <b>Number of subjects in period 1</b> | Omalizumab |
| Started                               | 38         |
| Completed                             | 38         |

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values    | Overall trial | Total |  |
|---------------------------|---------------|-------|--|
| Number of subjects        | 38            | 38    |  |
| Age categorical           |               |       |  |
| Units: Subjects           |               |       |  |
| Children (2-11 years)     | 21            | 21    |  |
| Adolescents (12-17 years) | 17            | 17    |  |
| Age continuous            |               |       |  |
| Units: years              |               |       |  |
| arithmetic mean           | 10.7          |       |  |
| standard deviation        | ± 2.46        | -     |  |
| Gender categorical        |               |       |  |
| Units: Subjects           |               |       |  |
| Female                    | 15            | 15    |  |
| Male                      | 23            | 23    |  |

## End points

### End points reporting groups

|  |            |
|--|------------|
| Reporting group title                                | Omalizumab |
| Reporting group description:<br>Omalizumab treatment |            |

### Primary: Geometric mean of serum free IgE level at 24 weeks

|  |   |
|--|---|
| End point title  | Geometric mean of serum free IgE level at 24 weeks <sup>[1]</sup> |
| End point description:<br>To evaluate whether the geometric mean of serum free IgE level at 24 weeks of the treatment period in Japanese pediatric patients reaches under 25 ng/mL (target level). |   |
| End point type   | Primary   |
| End point timeframe:<br>24 weeks   |   |

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: No statistical analyses have been specified for this primary end point.

| End point values                         | Omalizumab                |  |  |  |
|--|---------------------------|--|--|--|
| Subject group type                       | Reporting group           |  |  |  |
| Number of subjects analysed              | 38 <sup>[2]</sup>         |  |  |  |
| Units: ng/ml                             |                           |  |  |  |
| geometric mean (confidence interval 95%) | 15.551 (13.844 to 17.469) |  |  |  |

Notes:

[2] - Pharmacokinetic set:received study medication and and provided drug concentration data

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in peak expiratory flow (PEF)

|   |  |
|---|--|
| End point title   | Change from baseline in peak expiratory flow (PEF) |
| End point description:<br>PEF was measured at almost the same time in the morning and evening each day during the run-in and treatment period. The measurements were performed, using a Peak Flow Meter provided to the patients at Visit 1, within 15 minutes of wakening in the morning prior to rescue and asthma control medication use. The evening PEF was also measured prior to rescue and asthma control medication use. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline and 24 weeks   |  |

| End point values                     | Omalizumab        |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 38 <sup>[3]</sup> |  |  |  |
| Units: L/min                         |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| Morning PEF - Baseline               | 246.2 (± 72.22)   |  |  |  |
| Morning PEF - 24 weeks               | 269.3 (± 95.59)   |  |  |  |
| Morning PEF - Change from baseline   | 22.4 (± 60.59)    |  |  |  |
| Evening PEF - Baseline               | 255.4 (± 69.45)   |  |  |  |
| Evening PEF - 24 weeks               | 276.9 (± 93.38)   |  |  |  |
| Evening PEF - Change from baseline   | 21.5 (± 60.95)    |  |  |  |

Notes:

[3] - Full analysis set- n = 37, 38, 37, 38, 38, 38

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in FEV1 at 24 weeks

|   |  |
|---|--|
| End point title   | Change from baseline in FEV1 at 24 weeks |
| End point description:  |  |
| FEV1 was measured at almost the same time in the morning and evening each day during the run-in and treatment period. The measurements were performed, using a Peak Flow Meter provided to the patients at Visit 1, within 15 minutes of waking in the morning prior to rescue and asthma control medication use. The evening FEV1 was also measured prior to rescue and asthma control medication use. |  |
| End point type  | Secondary                                |
| End point timeframe:  |  |
| Baseline and 24 weeks   |  |

| End point values                     | Omalizumab        |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 38 <sup>[4]</sup> |  |  |  |
| Units: Liter                         |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| FEV1 - Baseline                      | 1.841 (± 0.4438)  |  |  |  |
| FEV1 - 24 weeks                      | 1.928 (± 0.5479)  |  |  |  |
| FEV1 - Change from baseline          | 0.087 (± 0.3314)  |  |  |  |

Notes:

[4] - Full analysis set

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Change from baseline in asthma symptom score, daily activity score, nocturnal sleep score at 24 weeks**

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|                 |   |
|-----------------|---|
| End point title | Change from baseline in asthma symptom score, daily activity score, nocturnal sleep score at 24 weeks |
|-----------------|---|

End point description:

The asthma symptoms and the cough were measured three times a day. The daily activity and the nocturnal sleep were measured once a day. From these measurements, asthma symptom score, daily activity score and nocturnal sleep score were calculated according to the rating standard of the Japanese Society of Allergology. The asthma symptom score in a day (possible range 0 to 30) was calculated by summing symptom scores (ranges 0 to 9) and cough scores (ranges 0 or 1) in the morning, the afternoon and the evening as recorded on the diary. The total activity score (ranges 0 to 27) was calculated as the total of daily activity score (ranges 0 to 18) and nocturnal sleep score (ranges 0 to 9).

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

End point timeframe:

Baseline and 24 weeks

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| End point values                             | Omalizumab        |  |  |  |
|--|-------------------|--|--|--|
| Subject group type                           | Reporting group   |  |  |  |
| Number of subjects analysed                  | 38 <sup>[5]</sup> |  |  |  |
| Units: Scores on a scale                     |                   |  |  |  |
| arithmetic mean (standard deviation)         |                   |  |  |  |
| Asthma symptom score - Baseline              | 21.9 (± 20.27)    |  |  |  |
| Asthma symptom score - 24 weeks              | 8.3 (± 11.48)     |  |  |  |
| Asthma symptom score - Change from baseline  | -13.6 (± 19.23)   |  |  |  |
| Daily activity score - Baseline              | 21 (± 17.87)      |  |  |  |
| Daily activity score - 24 weeks              | 3.9 (± 7.98)      |  |  |  |
| Daily activity score - Change from baseline  | -17.1 (± 17.9)    |  |  |  |
| Nocturnal sleep score - Baseline             | 9.2 (± 9.82)      |  |  |  |
| Nocturnal sleep score - 24 weeks             | 2.8 (± 6.39)      |  |  |  |
| Nocturnal sleep score - Change from baseline | -6.4 (± 11.29)    |  |  |  |

Notes:

[5] - Full analysis set

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Change from baseline in number of puffs/tablets of asthma rescue medication at 24 weeks**

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|                 |   |
|-----------------|---|
| End point title | Change from baseline in number of puffs/tablets of asthma rescue medication at 24 weeks |
|-----------------|---|

End point description:

The use of asthma rescue medication taken in a day was calculated by summing the number of puffs/tablets taken in the morning, noon and evening.

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

End point timeframe:  
Baseline and 24 weeks

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Omalizumab        |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 38 <sup>[6]</sup> |  |  |  |
| Units: Number of puffs               |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| Baseline                             | 6.6 (± 11.17)     |  |  |  |
| 24 weeks                             | 2.2 (± 4.82)      |  |  |  |
| Change from baseline                 | -4.4 (± 7.7)      |  |  |  |

Notes:

[6] - Full analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in quality of life score at 24 weeks

|  |   |
|--|---|
| End point title  | Change from baseline in quality of life score at 24 weeks |
| End point description:<br>Quality of life questionnaires for pediatric patients with bronchial asthma and their parents or caregivers were administered to all patients/their parents or guardians at Visits 2, 7 and 9 (or at discontinuation). The questionnaires was completed prior to any other visit assessments and study drug administration to avoid influencing the responses. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline and 24 weeks  |   |

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Omalizumab        |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 37 <sup>[7]</sup> |  |  |  |
| Units: Scores on a scale             |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| 24 weeks vs baseline - Baseline      | 23 (± 5.01)       |  |  |  |
| 24 weeks vs baseline - Post-baseline | 26.2 (± 5.19)     |  |  |  |
| Emotional - Baseline                 | 15.1 (± 3.08)     |  |  |  |
| Emotional - Post-baseline            | 17.3 (± 3.04)     |  |  |  |
| Overall - Baseline                   | 38.1 (± 7.33)     |  |  |  |
| Overall - Post-baseline              | 43.5 (± 7.55)     |  |  |  |

Notes:

[7] - Full analysis set

### Statistical analyses



No statistical analyses for this end point

## Secondary: Investigators Global Evaluation of Treatment Effectiveness (GETE)s and patients GETEs at 24 weeks

|                 |   |
|-----------------|---|
| End point title | Investigators Global Evaluation of Treatment Effectiveness (GETE)s and patients GETEs at 24 weeks |
|-----------------|---|

End point description:

The global evaluation of the treatment effectiveness performed by the investigator and the patient and evaluated based on the following scale:

1. Excellent (complete control of asthma)
2. Good (marked improvement of asthma)
3. Moderate (discernible, but limited improvement in asthma)
4. Poor (no appreciable change in asthma)
5. Worsening of asthma

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

End point timeframe:

24 weeks /the last assessment

| End point values               | Omalizumab        |  |  |  |
|--------------------------------|-------------------|--|--|--|
| Subject group type             | Reporting group   |  |  |  |
| Number of subjects analysed    | 38 <sup>[8]</sup> |  |  |  |
| Units: percent                 |                   |  |  |  |
| number (not applicable)        |                   |  |  |  |
| Investigators GETE - Excellent | 7.9               |  |  |  |
| Investigators GETE - Good      | 68.4              |  |  |  |
| Investigators GETE - Moderate  | 23.7              |  |  |  |
| Investigators GETE - Poor      | 0                 |  |  |  |
| Investigators GETE - Worsening | 0                 |  |  |  |
| Patients GETE - Excellent      | 31.6              |  |  |  |
| Patients GETE - Good           | 47.4              |  |  |  |
| Patients GETE - Moderate       | 15.8              |  |  |  |
| Patients GETE - Poor           | 5.3               |  |  |  |
| Patients GETE - Worsening      | 0                 |  |  |  |

Notes:

[8] - Full analysis set

## 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 reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 14.1   |

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Omalizumab |
|-----------------------|------------|

Reporting group description:

Omalizumab

| Serious adverse events                            | Omalizumab      |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 6 / 38 (15.79%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |
| Respiratory, thoracic and mediastinal disorders   |                 |  |  |
| Asthma  |                 |  |  |
| subjects affected / exposed                       | 5 / 38 (13.16%) |  |  |
| occurrences causally related to treatment / all   | 1 / 5           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders            |                 |  |  |
| Urticaria   |                 |  |  |
| subjects affected / exposed                       | 1 / 38 (2.63%)  |  |  |
| occurrences causally related to treatment / all   | 1 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |

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

| Non-serious adverse events                            | Omalizumab       |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 36 / 38 (94.74%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |

|  |   |  |  |
|--|---|--|--|
| Contusion<br>subjects affected / exposed<br>occurrences (all)  | 3 / 38 (7.89%)<br>4   |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 5 / 38 (13.16%)<br>7  |  |  |
| General disorders and administration<br>site conditions<br>Injection site erythema<br>subjects affected / exposed<br>occurrences (all)<br><br>Injection site pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Injection site swelling<br>subjects affected / exposed<br>occurrences (all)<br><br>Malaise<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 2 / 38 (5.26%)<br>3<br><br>3 / 38 (7.89%)<br>7<br><br>2 / 38 (5.26%)<br>3<br><br>2 / 38 (5.26%)<br>3<br><br>3 / 38 (7.89%)<br>3 |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Stomatitis<br>subjects affected / exposed<br>occurrences (all)   | 4 / 38 (10.53%)<br>5<br><br>3 / 38 (7.89%)<br>3<br><br>4 / 38 (10.53%)<br>4   |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Asthma   |   |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>4 / 38 (10.53%)</p> <p>4</p> <p>2 / 38 (5.26%)</p> <p>2</p>  |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Eczema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>2 / 38 (5.26%)</p> <p>2</p> <p>4 / 38 (10.53%)</p> <p>5</p>  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>3 / 38 (7.89%)</p> <p>4</p> <p>2 / 38 (5.26%)</p> <p>2</p>   |  |  |
| <p>Infections and infestations</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastroenteritis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Influenza</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sinusitis</p> | <p>5 / 38 (13.16%)</p> <p>9</p> <p>8 / 38 (21.05%)</p> <p>9</p> <p>3 / 38 (7.89%)</p> <p>3</p> <p>10 / 38 (26.32%)</p> <p>13</p> <p>2 / 38 (5.26%)</p> <p>2</p> |  |  |

|                                    |                  |  |  |
|------------------------------------|------------------|--|--|
| subjects affected / exposed        | 2 / 38 (5.26%)   |  |  |
| occurrences (all)                  | 2                |  |  |
| Upper respiratory tract infection  |                  |  |  |
| subjects affected / exposed        | 10 / 38 (26.32%) |  |  |
| occurrences (all)                  | 14               |  |  |
| Metabolism and nutrition disorders |                  |  |  |
| Decreased appetite                 |                  |  |  |
| subjects affected / exposed        | 2 / 38 (5.26%)   |  |  |
| occurrences (all)                  | 2                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment   |
|----------------|---|
| 23 August 2011 | <ul style="list-style-type: none"><li>• Changed the bioanalytical CRO for total IgE analysis from Phadia to Atlanbio due to business considerations.</li><li>• Updated information on storage condition of reconstituted study medication due to the technical change.</li><li>• Added an alternative instruction for calibration of spirometers due to the technical change.</li><li>• Deleted the process of obvious errors correction and corrected the way to change the database after it is locked.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported