

**Clinical trial results:****Effect of Low Dose Continuous Treatment with Ciclesonide over One Year on the Time to First Exacerbation in Children with Mild Asthma Versus Intermittent Treatment for Exacerbations****Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2007-003736-34 |
| Trial protocol           | HU             |
| Global end of trial date | 25 June 2009   |

**Results information**

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 28 May 2017  |
| First version publication date | 28 May 2017  |

**Trial information****Trial identification**

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | BY9010/CA-101 |
|-----------------------|---------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00163293 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AstraZeneca   |
| Sponsor organisation address | One MedImmune Way, Gaithersburg, United States, 20878   |
| Public contact               | AstraZeneca Clinical Study Information Center, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact           | AstraZeneca Clinical Study Information Center, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |

Notes:

**Paediatric regulatory details**

|  |     |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP)       |     |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |
| 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                       | 25 June 2009 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 01 June 2009 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 25 June 2009 |
| Was the trial ended prematurely?                     | No           |

Notes:

---

**General information about the trial**

---

Main objective of the trial:

The aim of this study is to compare the efficacy of ciclesonide with respect to reduction of the number of asthma exacerbations in children with mild persistent asthma. Treatment medication will be administered as follows: ciclesonide will be inhaled once daily, using one of the two dose levels versus placebo together with other corticosteroids used as intermittent treatment. The study duration consists of a baseline period (3 to 4 weeks) and a treatment period (12 months). The study will provide further data on safety and tolerability of ciclesonide.

Protection of trial subjects:

All study participants or their representative were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 24 January 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 | Canada: 142      |
| Country: Number of subjects enrolled | Hungary: 39      |
| Country: Number of subjects enrolled | South Africa: 59 |
| Worldwide total number of subjects   | 240              |
| EEA total number of subjects         | 39               |

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)                     | 240 |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 0   |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 30 investigative sites in Canada, Hungary and South Africa from 24 January 2005 to 25 June 2009.

### Pre-assignment

Screening details:

Children who experienced symptoms consistent with mild asthma for at least 12 months were enrolled in 1 of 3 treatment groups: once a day placebo, 100 µg or 200 µg ciclesonide.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 240 |
| Number of subjects completed | 239 |

### Pre-assignment subject non-completion reasons

|                            |                                |
|----------------------------|--------------------------------|
| Reason: Number of subjects | Did not receive study drug.: 1 |
|----------------------------|--------------------------------|

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator, Carer   |

### Arms

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

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Ciclesonide 100 µg |
|------------------|--------------------|

Arm description:

Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

|  |                             |
|--|-----------------------------|
| Arm type                               | Experimental                |
| Investigational medicinal product name | Ciclesonide 100 µg          |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Inhalation vapour, solution |
| Routes of administration               | Inhalation use              |

Dosage and administration details:

50 µg two puffs once daily, in the evening via a metered-dose inhaler (50 µg ex-valve corresponds to 40 µg ex-actuator)

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Ciclesonide 200 µg |
|------------------|--------------------|

Arm description:

Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

|  |                             |
|--|-----------------------------|
| Arm type                               | Experimental                |
| Investigational medicinal product name | Ciclesonide 200 µg          |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Inhalation vapour, solution |
| Routes of administration               | Inhalation use              |

Dosage and administration details:

100 µg two puffs once daily, in the evening via a metered-dose inhaler (100 µg ex-valve corresponds to 80 µg ex-actuator)

|  |                              |
|--|------------------------------|
| <b>Arm title</b>   | Placebo                      |
| Arm description:<br>Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months. |                              |
| Arm type   | Placebo                      |
| Investigational medicinal product name   | Placebo-matching ciclesonide |
| Investigational medicinal product code   |                              |
| Other name   |                              |
| Pharmaceutical forms   | Inhalation vapour, solution  |
| Routes of administration   | Inhalation use               |

Dosage and administration details:

two puffs once daily, in the evening, via a metered-dose inhaler

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo |
|---|--------------------|--------------------|---------|
| Started   | 79                 | 76                 | 84      |
| Completed   | 66                 | 69                 | 66      |
| Not completed                                       | 13                 | 7                  | 18      |
| Reasons Not Specified                               | 13                 | 7                  | 18      |

Notes:

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

Justification: 240 patients were randomized but only 239 were treated.

## Baseline characteristics

### Reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Ciclesonide 100 µg |
| Reporting group description:<br>Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.           |                    |
| Reporting group title  | Ciclesonide 200 µg |
| Reporting group description:<br>Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.           |                    |
| Reporting group title  | Placebo            |
| Reporting group description:<br>Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months. |                    |

| Reporting group values  | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo |
|---|--------------------|--------------------|---------|
| Number of subjects  | 79                 | 76                 | 84      |
| Age categorical<br>Units: Subjects  |                    |                    |         |
| Children (2-11 years)   | 79                 | 76                 | 84      |
| Age Continuous<br>Units: years  |                    |                    |         |
| arithmetic mean   | 7.9                | 7.7                | 8.1     |
| standard deviation  | ± 2.06             | ± 1.84             | ± 2.19  |
| Gender, Male/Female<br>Units: participants                                  |                    |                    |         |
| Female  | 33                 | 31                 | 34      |
| Male  | 46                 | 45                 | 50      |
| Race/Ethnicity, Customized<br>Units: Subjects                               |                    |                    |         |
| Asian   | 6                  | 6                  | 6       |
| Black   | 4                  | 2                  | 5       |
| Caucasian   | 55                 | 53                 | 59      |
| Other   | 14                 | 15                 | 14      |
| Smoking Classification<br>Units: Subjects                                   |                    |                    |         |
| Non-Smokers   | 79                 | 76                 | 84      |
| Study Specific Characteristic   Weight                                      |                    |                    |         |
| Weight data was only available for n=77, 76, 84 participants, respectively. |                    |                    |         |
| Units: kg   |                    |                    |         |
| arithmetic mean   | 29.9               | 30.01              | 33.13   |
| standard deviation  | ± 9.701            | ± 9.247            | ± 11.64 |
| Study Specific Characteristic   Body Mass Index (BMI)                       |                    |                    |         |
| BMI data was only available for n=77, 76, 84 participants, respectively.    |                    |                    |         |
| Units: kg/m <sup>2</sup>  |                    |                    |         |
| arithmetic mean   | 17.3               | 17.69              | 18.68   |
| standard deviation  | ± 3.107            | ± 2.977            | ± 4.069 |
| <b>Reporting group values</b>   | Total              |                    |         |

|   |     |  |  |
|---|-----|--|--|
| Number of subjects  | 239 |  |  |
| Age categorical   |     |  |  |
| Units: Subjects   |     |  |  |
| Children (2-11 years)   | 239 |  |  |
| Age Continuous  |     |  |  |
| Units: years  |     |  |  |
| arithmetic mean   |     |  |  |
| standard deviation  | -   |  |  |
| Gender, Male/Female   |     |  |  |
| Units: participants   |     |  |  |
| Female  | 98  |  |  |
| Male  | 141 |  |  |
| Race/Ethnicity, Customized  |     |  |  |
| Units: Subjects   |     |  |  |
| Asian   | 18  |  |  |
| Black   | 11  |  |  |
| Caucasian   | 167 |  |  |
| Other   | 43  |  |  |
| Smoking Classification  |     |  |  |
| Units: Subjects   |     |  |  |
| Non-Smokers   | 239 |  |  |
| Study Specific Characteristic   Weight                                      |     |  |  |
| Weight data was only available for n=77, 76, 84 participants, respectively. |     |  |  |
| Units: kg   |     |  |  |
| arithmetic mean   |     |  |  |
| standard deviation  | -   |  |  |
| Study Specific Characteristic   Body Mass Index (BMI)                       |     |  |  |
| BMI data was only available for n=77, 76, 84 participants, respectively.    |     |  |  |
| Units: kg/m <sup>2</sup>  |     |  |  |
| arithmetic mean   |     |  |  |
| standard deviation  | -   |  |  |

## End points

### End points reporting groups

|                              |  |
|------------------------------|--|
| Reporting group title        | Ciclesonide 100 µg   |
| Reporting group description: | Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.           |
| Reporting group title        | Ciclesonide 200 µg   |
| Reporting group description: | Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.           |
| Reporting group title        | Placebo  |
| Reporting group description: | Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months. |

### Primary: Time to First Asthma Exacerbation

|                        |   |
|------------------------|---|
| End point title        | Time to First Asthma Exacerbation   |
| End point description: | Time to first asthma exacerbation is defined as the time in days until the first asthma exacerbation, or to the end of treatment visit. In the absence of an exacerbation, an early treatment discontinuation is treated as a censored observation on the day following the last use of study drug. Intention to Treat (ITT) analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. |
| End point type         | Primary   |
| End point timeframe:   | Up to 12 months   |

| End point values                 | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|----------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type               | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed      | 79                 | 76                 | 84              |  |
| Units: days                      |                    |                    |                 |  |
| arithmetic mean (standard error) | 225.1 (± 14.73)    | 249.5 (± 14.79)    | 227.2 (± 15.2)  |  |

### Statistical analyses

|   |                              |
|---|------------------------------|
| Statistical analysis title              | Analysis 1                   |
| Comparison groups                       | Ciclesonide 100 µg v Placebo |
| Number of subjects included in analysis | 163                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.6625                     |
| Method                                  | Logrank                      |

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Analysis 2                   |
| Comparison groups                       | Ciclesonide 200 µg v Placebo |
| Number of subjects included in analysis | 160                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.7303                     |
| Method                                  | Logrank                      |

### Primary: Exacerbations (Post-hoc Analysis of Annual Rates)

|   |   |
|---|---|
| End point title   | Exacerbations (Post-hoc Analysis of Annual Rates) |
| End point description:  |   |
| <p>A model-based analysis of asthma exacerbation was performed to adjust to important covariables. The distribution of the data suggested a Poisson regression modeling (zero inflated) strategy. After a variable selection process considering also variable-by-treatment interactions, the variables centre, age [years] and race were identified to be important beside treatment. The parameters centre and age [years] were allocated to zero-model part and the variables treatment and race to the Poisson model part. The estimates of the per-treatment rates are based on a negative-binomial distribution. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.</p> |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Up to 12 months   |   |

| End point values                    | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo           |  |
|-------------------------------------|--------------------|--------------------|-------------------|--|
| Subject group type                  | Reporting group    | Reporting group    | Reporting group   |  |
| Number of subjects analysed         | 79                 | 76                 | 84                |  |
| Units: number of events per year    |                    |                    |                   |  |
| least squares mean (standard error) | 0.9343 (± 0.2909)  | 0.8794 (± 0.2747)  | 1.2621 (± 0.2768) |  |

### Statistical analyses

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Analysis 1                   |
| Comparison groups                       | Ciclesonide 100 µg v Placebo |
| Number of subjects included in analysis | 163                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.1291 <sup>[1]</sup>      |
| Method                                  | Wald Chi-square              |

Notes:

[1] - zero inflated Poisson model: adjustment for centre and age [yrs] (zero model), treatment and race (Poisson model)

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Analysis 2                   |
| Comparison groups                       | Ciclesonide 200 µg v Placebo |
| Number of subjects included in analysis | 160                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.0145 [2]                 |
| Method                                  | Wald Chi-square              |

Notes:

[2] - zero inflated Poisson model: adjustment for centre and age [yrs] (zero model), treatment and race (Poisson model)

### **Secondary: Growth Velocity as Assessed by Stadiometric Height Measurement**

|                 |  |
|-----------------|--|
| End point title | Growth Velocity as Assessed by Stadiometric Height Measurement |
|-----------------|--|

End point description:

Standing height measured in millimeters (mm) with a wall-mounted stadiometer. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>              | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 79                 | 76                 | 84              |  |
| Units: mm/year                       |                    |                    |                 |  |
| arithmetic mean (standard deviation) | 55.32 (± 25.81)    | 64.6 (± 27.31)     | 54.91 (± 21.78) |  |

### **Statistical analyses**

No statistical analyses for this end point

### **Secondary: Mean Rate of Asthma Exacerbations per Year**

|                 |  |
|-----------------|--|
| End point title | Mean Rate of Asthma Exacerbations per Year |
|-----------------|--|

End point description:

Rate of asthma exacerbations per year is equal to total number of asthma exacerbations during treatment/time on treatment (year). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>                 | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|---|--------------------|--------------------|-----------------|--|
| Subject group type                      | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed             | 79                 | 76                 | 84              |  |
| Units: number of exacerbations per year |                    |                    |                 |  |
| arithmetic mean (standard deviation)    | 0.88 (± 1.366)     | 0.85 (± 1.31)      | 3.28 (± 19.874) |  |

### Statistical analyses

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Analysis 2                   |
| Comparison groups                       | Ciclesonide 200 µg v Placebo |
| Number of subjects included in analysis | 160                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.6844                     |
| Method                                  | Kruskal-wallis               |

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Analysis 1                   |
| Comparison groups                       | Ciclesonide 100 µg v Placebo |
| Number of subjects included in analysis | 163                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.4754                     |
| Method                                  | Kruskal-wallis               |

### Secondary: Duration of Exacerbations

|                        |  |
|------------------------|--|
| End point title        | Duration of Exacerbations  |
| End point description: | Duration of exacerbation was defined as the time in days when the criteria for an exacerbation were met to the time when peak flow measurements returned to baseline. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. |
| End point type         | Secondary  |
| End point timeframe:   | Up to 12 months  |

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 79                    | 76                    | 84              |  |
| Units: days                          |                       |                       |                 |  |
| arithmetic mean (standard deviation) | 9.17 (± 6.198)        | 9.31 (± 7.65)         | 7.92 (± 4.061)  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Exacerbations per Participant

|                 |   |
|-----------------|---|
| End point title | Number of Exacerbations per Participant |
|-----------------|---|

End point description:

The mean number of asthma exacerbations per participant is reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 79                    | 76                    | 84              |  |
| Units: exacerbations                 |                       |                       |                 |  |
| arithmetic mean (standard deviation) | 0.72 (± 1.025)        | 0.78 (± 1.028)        | 0.95 (± 1.316)  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants who Dropped-out due to Asthma Exacerbation

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Dropped-out due to Asthma Exacerbation |
|-----------------|---|

End point description:

ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>           | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|-----------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed       | 79                    | 76                    | 84              |  |
| Units: percentage of participants |                       |                       |                 |  |
| number (not applicable)           | 1.3                   | 1.3                   | 4.8             |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Absolute Value)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Absolute Value) |
|-----------------|--|

End point description:

FEV1 is the maximal amount of air forcefully exhaled from the lungs in one second. Spirometry was used for assessment of FEV1. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo             |  |
|--------------------------------------|-----------------------|-----------------------|---------------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group     |  |
| Number of subjects analysed          | 79                    | 76                    | 84                  |  |
| Units: liters                        |                       |                       |                     |  |
| arithmetic mean (standard deviation) |                       |                       |                     |  |
| Change at Month 1 (n=78, 76, 81)     | 0.019 (±<br>0.1715)   | 0.018 (±<br>0.1639)   | 0.012 (±<br>0.1627) |  |
| Change at Month 2 (n=76, 73, 77)     | 0.024 (±<br>0.1416)   | 0.06 (±<br>0.1582)    | 0.005 (±<br>0.1416) |  |
| Change at Month 4 (n=68, 72, 75)     | 0.065 (±<br>0.1483)   | 0.083 (±<br>0.1486)   | 0.076 (±<br>0.1725) |  |
| Change at Month 6 (n=67, 72, 72)     | 0.091 (±<br>0.1714)   | 0.125 (±<br>0.1975)   | 0.078 (±<br>0.1855) |  |
| Change at Month 8 (n=66, 71, 68)     | 0.075 (±<br>0.2144)   | 0.126 (±<br>0.2089)   | 0.12 (±<br>0.1855)  |  |
| Change at Month 10 (n=66, 69, 67)    | 0.143 (±<br>0.1458)   | 0.168 (±<br>0.191)    | 0.146 (±<br>0.1609) |  |
| Change at Month 12 (n=65, 69, 65)    | 0.161 (±<br>0.2022)   | 0.185 (±<br>0.2024)   | 0.178 (±<br>0.1593) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Percent Predicted)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Percent Predicted) |
|-----------------|---|

End point description:

FEV1 is the maximal amount of air forcefully exhaled from the lungs in one second. Spirometry was used for assessment of FEV1. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 79                 | 76                 | 84              |  |
| Units: percent predicted FEV1        |                    |                    |                 |  |
| arithmetic mean (standard deviation) |                    |                    |                 |  |
| Change at Month 1 (n=78, 76, 81)     | 1 (± 10.96)        | 0.6 (± 9.67)       | 1 (± 9.06)      |  |
| Change at Month 2 (n=76, 73, 77)     | 1.4 (± 8.5)        | 3.4 (± 9.6)        | 0.3 (± 8.05)    |  |
| Change at Month 4 (n=68, 72, 75)     | 4 (± 8.69)         | 4.6 (± 9.31)       | 5.1 (± 9.83)    |  |
| Change at Month 6 (n=67, 72, 72)     | 5.5 (± 10)         | 7.2 (± 11.35)      | 4.9 (± 10.93)   |  |
| Change at Month 8 (n=66, 71, 68)     | 4.4 (± 12.44)      | 6.5 (± 12.25)      | 7.1 (± 10.24)   |  |
| Change at Month 10 (n=66, 69, 67)    | 8.6 (± 9.41)       | 9.1 (± 10.48)      | 8.7 (± 9.22)    |  |
| Change at Month 12 (n=65, 69, 65)    | 9.5 (± 10.96)      | 10.1 (± 11.29)     | 10.4 (± 9.89)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Morning and Evening Peak Expiratory Flow (PEF) Measurements by Diary Entries

|                 |  |
|-----------------|--|
| End point title | Morning and Evening Peak Expiratory Flow (PEF) Measurements by Diary Entries |
|-----------------|--|

End point description:

PEF is the maximum speed of expiration. Spirometry was used for assessment of PEF. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo              |  |
|--------------------------------------|-----------------------|-----------------------|----------------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group      |  |
| Number of subjects analysed          | 79                    | 76                    | 84                   |  |
| Units: liters/second                 |                       |                       |                      |  |
| arithmetic mean (standard deviation) |                       |                       |                      |  |
| Month 1, Evening PEF (n=78, 76, 80)  | 235.72 (±<br>63.882)  | 238.16 (±<br>52.565)  | 241.89 (±<br>70.619) |  |
| Month 1, Morning PEF (n=78, 76, 81)  | 232.09 (±<br>64.933)  | 234.41 (±<br>52.908)  | 233.81 (±<br>66.039) |  |
| Month 2, Evening PEF (n=76, 71, 77)  | 241.07 (±<br>58.604)  | 241.16 (±<br>50.422)  | 244.67 (±<br>67.846) |  |
| Month 2, Morning PEF (n=76, 72, 77)  | 236.92 (±<br>61.243)  | 236.42 (±<br>52.323)  | 239.07 (±<br>70.132) |  |
| Month 4, Evening PEF (n=68, 72, 75)  | 249.75 (±<br>58.528)  | 243.52 (±<br>49.076)  | 245.91 (±<br>65.802) |  |
| Month 4, Morning PEF (n=68, 71, 76)  | 242.93 (±<br>56.658)  | 241.91 (±<br>48.498)  | 240.16 (±<br>65.211) |  |
| Month 6, Evening PEF (n=67, 72, 73)  | 251.88 (±<br>60.255)  | 249.36 (±<br>59.294)  | 246.44 (±<br>63.946) |  |
| Month 6, Morning PEF (n=67, 72, 73)  | 246.44 (±<br>59.781)  | 246.75 (±<br>60.02)   | 238.81 (±<br>63.419) |  |
| Month 8, Evening PEF (n=66, 70, 69)  | 253.49 (±<br>59.666)  | 250.92 (±<br>51.376)  | 245.72 (±<br>61.399) |  |
| Month 8, Morning PEF (n=66, 71, 69)  | 247.24 (±<br>59.806)  | 246.97 (±<br>51.592)  | 239.73 (±<br>61.733) |  |
| Month 10, Evening PEF (n=65, 70, 68) | 254.21 (±<br>56.815)  | 256.44 (±<br>56.469)  | 251.69 (±<br>60.704) |  |
| Month 10, Morning PEF (n=66, 70, 68) | 247.94 (±<br>60.418)  | 254.04 (±<br>56.719)  | 246.23 (±<br>62.805) |  |
| Month 12, Evening PEF (n=68, 71, 70) | 255.97 (±<br>57.291)  | 263.87 (±<br>58.469)  | 261.88 (±<br>61.383) |  |
| Month 12, Morning PEF (n=75, 73, 78) | 245.84 (±<br>59.834)  | 258.62 (±<br>57.009)  | 250.55 (±<br>63.204) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in PEF by Diary Entries

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in PEF by Diary Entries |
|-----------------|--|

End point description:

PEF is the maximum speed of expiration. Spirometry was used for assessment of PEF. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

| <b>End point values</b>                        | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo          |  |
|--|-----------------------|-----------------------|------------------|--|
| Subject group type                             | Reporting group       | Reporting group       | Reporting group  |  |
| Number of subjects analysed                    | 79                    | 76                    | 84               |  |
| Units: liters/second                           |                       |                       |                  |  |
| arithmetic mean (standard deviation)           |                       |                       |                  |  |
| Change at Month 1, Evening PEF (n=78, 76, 80)  | 8.46 (± 17.952)       | 8.54 (± 19.474)       | 6.06 (± 39.183)  |  |
| Change at Month 1, Morning PEF (n=78, 76, 81)  | 11.69 (± 21.268)      | 10.82 (± 20.372)      | 7.54 (± 25.697)  |  |
| Change at Month 2, Evening PEF (n=76, 71, 77)  | 13.66 (± 28.491)      | 13.04 (± 20.89)       | 10.83 (± 40.563) |  |
| Change at Month 2, Morning PEF (n=76, 72, 77)  | 17.12 (± 32.068)      | 14.3 (± 22.649)       | 14.29 (± 37.228) |  |
| Change at Month 4, Evening PEF (n=68, 72, 75)  | 20.41 (± 22.058)      | 16.01 (± 21.547)      | 13.62 (± 37.99)  |  |
| Change at Month 4, Morning PEF (n=68, 71, 76)  | 21.33 (± 26.603)      | 18.24 (± 22.808)      | 16.28 (± 34.841) |  |
| Change at Month 6, Evening PEF (n=67, 72, 73)  | 22.44 (± 28.236)      | 21.86 (± 38.28)       | 13.14 (± 33.321) |  |
| Change at Month 6, Morning PEF (n=67, 72, 73)  | 24.82 (± 30.613)      | 24.68 (± 40.981)      | 14.44 (± 29.95)  |  |
| Change at Month 8, Evening PEF (n=66, 70, 69)  | 25.47 (± 27.43)       | 21.38 (± 28.648)      | 13.3 (± 37.061)  |  |
| Change at Month 8, Morning PEF (n=66, 71, 69)  | 27.16 (± 32.53)       | 23.76 (± 29.089)      | 16.03 (± 34.017) |  |
| Change at Month 10, Evening PEF (n=65, 70, 68) | 25.68 (± 30.945)      | 26.78 (± 34.255)      | 18.04 (± 38.209) |  |
| Change at Month 10, Morning PEF (n=66, 70, 68) | 27.86 (± 38.406)      | 29.84 (± 36.39)       | 21.25 (± 34.94)  |  |
| Change at Month 12, Evening PEF (n=68, 71, 70) | 28.24 (± 28.811)      | 33.35 (± 38.772)      | 25.38 (± 43.284) |  |
| Change at Month 12, Morning PEF (n=75, 73, 78) | 26.84 (± 32.932)      | 34.31 (± 41.166)      | 24.37 (± 39.312) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Diurnal PEF Fluctuation

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Diurnal PEF Fluctuation |
|-----------------|---|

End point description:

Diurnal PEF Fluctuation is equal to  $[(\text{Higher PEF} - \text{Lower PEF}) / 0.5 * (\text{Higher PEF} + \text{Lower PEF})] * 100\%$ . A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 79                    | 76                    | 84              |  |
| Units: percent fluctuation           |                       |                       |                 |  |
| arithmetic mean (standard deviation) |                       |                       |                 |  |
| Change at Month 1 (n=78, 76, 80)     | -0.59 (± 3.97)        | 0.06 (± 3.772)        | 0 (± 3.867)     |  |
| Change at Month 2 (n=76, 71, 77)     | -0.13 (± 5.009)       | -0.16 (± 4.131)       | 0.15 (± 5.084)  |  |
| Change at Month 4 (n=68, 71, 75)     | -0.65 (± 5.251)       | -1.01 (± 3.784)       | -0.55 (± 4.421) |  |
| Change at Month 6 (n=67, 72, 73)     | -1.01 (± 4.351)       | -0.22 (± 5.86)        | -0.47 (± 4.28)  |  |
| Change at Month 8 (n=66, 70, 69)     | -1.12 (± 4.83)        | -1.21 (± 3.757)       | -1.11 (± 4.048) |  |
| Change at Month 10 (n=64, 70, 68)    | -1.46 (± 5.221)       | -0.7 (± 4.319)        | -1.14 (± 4.059) |  |
| Change at Month 12 (n=68, 70, 70)    | -1.81 (± 4.913)       | -0.62 (± 4.44)        | -1.26 (± 4.187) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Total Asthma Symptom Score by Diary Entries

|                        |  |
|------------------------|--|
| End point title        | Total Asthma Symptom Score by Diary Entries  |
| End point description: | Total Asthma Score=daytime asthma score + night-time asthma score, where higher score indicates worsening of disease. Night-time asthma score is assessed on a 5 point scale where 0=No symptoms, slept through the night, 1=Slept well but some complaints in the morning, 2=Woke up once because of asthma (including early wakening), 3=Woke up several times because of asthma (including early wakening) and 4=Bad night, awake most of the night because of asthma. Day-time asthma score is assessed on a 5 point scale where 0=Very well, no symptoms, 1=one episode of wheezing, cough or breathlessness, 2=More than 1 episode of wheezing, cough or breathlessness without interfering with normal activities, 3=Wheezing, cough or shortness of breath most of the day which interfered to some extent with normal activities and 4=Asthma very bad. Unable to carry out daily activities as usual. ITT analysis. "n" in the category is the number of participants with data available at the given time-point. |
| End point type         | Secondary  |
| End point timeframe:   | Months 1, 2, 4, 6, 8, 10 and 12  |

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 79                    | 76                    | 84              |  |
| Units: score on a scale              |                       |                       |                 |  |
| arithmetic mean (standard deviation) |                       |                       |                 |  |
| Month 1 (n=77, 75, 79)               | 0.37 (± 0.489)        | 0.22 (± 0.329)        | 0.32 (± 0.535)  |  |

|                         |                |                |                |
|-------------------------|----------------|----------------|----------------|
| Month 2 (n=76, 70, 77)  | 0.26 (± 0.424) | 0.14 (± 0.246) | 0.28 (± 0.484) |
| Month 4 (n=68, 72, 75)  | 0.18 (± 0.342) | 0.12 (± 0.178) | 0.24 (± 0.359) |
| Month 6 (n=67, 72, 73)  | 0.16 (± 0.289) | 0.17 (± 0.294) | 0.18 (± 0.289) |
| Month 8 (n=66, 69, 69)  | 0.17 (± 0.283) | 0.13 (± 0.243) | 0.23 (± 0.414) |
| Month 10 (n=64, 70, 68) | 0.12 (± 0.253) | 0.11 (± 0.227) | 0.24 (± 0.49)  |
| Month 12 (n=68, 69, 70) | 0.11 (± 0.24)  | 0.08 (± 0.129) | 0.15 (± 0.338) |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Nights with Nocturnal Awakenings due to Asthma Symptoms

|                 |   |
|-----------------|---|
| End point title | Percentage of Nights with Nocturnal Awakenings due to Asthma Symptoms |
|-----------------|---|

End point description:

Nocturnal awakenings due to asthma symptoms were recorded in the participant's diary. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |
|--------------------------------------|--------------------|--------------------|-----------------|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |
| Number of subjects analysed          | 79                 | 76                 | 84              |
| Units: percentage of nights          |                    |                    |                 |
| arithmetic mean (standard deviation) |                    |                    |                 |
| Month 1 (n=78, 75, 80)               | 2.4 (± 6.159)      | 1.64 (± 4.256)     | 1.85 (± 4.223)  |
| Month 2 (n=76, 73, 77)               | 1.96 (± 5.877)     | 0.62 (± 2.364)     | 1.73 (± 4.662)  |
| Month 4 (n=68, 72, 75)               | 1.33 (± 4.017)     | 0.86 (± 2.139)     | 1.54 (± 4.106)  |
| Month 6 (n=67, 72, 73)               | 0.87 (± 2.527)     | 1.51 (± 3.288)     | 1.26 (± 3.235)  |
| Month 8 (n=66, 70, 69)               | 1.62 (± 4.129)     | 1.05 (± 2.823)     | 1.82 (± 5.024)  |
| Month 10 (n=66, 70, 68)              | 1.93 (± 7.106)     | 0.59 (± 2.22)      | 1.88 (± 5.468)  |
| Month 12 (n=74, 73, 78)              | 0.41 (± 1.554)     | 1.84 (± 11.769)    | 0.53 (± 1.853)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Rescue Medication Use per Day

|                 |                               |
|-----------------|-------------------------------|
| End point title | Rescue Medication Use per Day |
|-----------------|-------------------------------|

End point description:

Salbutamol (100 µg/puff) was used as rescue medication according to the individual needs of the participant. Each use was documented in the participant's diary. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 79                 | 76                 | 84              |  |
| Units: puffs/day                     |                    |                    |                 |  |
| arithmetic mean (standard deviation) |                    |                    |                 |  |
| Month 1 (n=57, 51, 54)               | 1 (± 1.345)        | 0.83 (± 1.148)     | 0.87 (± 0.91)   |  |
| Month 2 (n=53, 40, 46)               | 0.99 (± 1.296)     | 0.53 (± 0.728)     | 0.97 (± 1.298)  |  |
| Month 4 (n=48, 47, 51)               | 0.88 (± 1.3)       | 1.18 (± 1.595)     | 1.27 (± 1.984)  |  |
| Month 6 (n=45, 43, 44)               | 0.79 (± 1.084)     | 1.07 (± 1.329)     | 0.92 (± 1.583)  |  |
| Month 8 (n=38, 42, 45)               | 1.01 (± 1.53)      | 1.13 (± 1.95)      | 0.97 (± 1.219)  |  |
| Month 10 (n=38, 41, 39)              | 0.93 (± 1.423)     | 0.95 (± 1.243)     | 0.83 (± 1.113)  |  |
| Month 12 (n=36, 40, 40)              | 0.71 (± 0.897)     | 1.01 (± 1.36)      | 0.75 (± 1.152)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Rescue Medication Free Days

End point title Percentage of Rescue Medication Free Days

End point description:

Days without use of rescue medication documented in the participant's diary were reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 79                 | 76                 | 84              |  |
| Units: percentage of days            |                    |                    |                 |  |
| arithmetic mean (standard deviation) |                    |                    |                 |  |

|                         |                  |                  |                  |
|-------------------------|------------------|------------------|------------------|
| Month 1 (n=55, 53, 54)  | 47.94 (± 44.405) | 47.34 (± 44.984) | 44.37 (± 45.367) |
| Month 2 (n=52, 41, 48)  | 48.78 (± 46.442) | 54.46 (± 46.668) | 45.31 (± 47.761) |
| Month 4 (n=49, 48, 52)  | 49.91 (± 48.274) | 46.51 (± 45.209) | 45.91 (± 46.328) |
| Month 6 (n=47, 44, 45)  | 49.63 (± 48.084) | 48.14 (± 45.321) | 49.42 (± 47.515) |
| Month 8 (n=39, 42, 44)  | 47.93 (± 45.17)  | 50.5 (± 46.1)    | 45.22 (± 45.002) |
| Month 10 (n=40, 40, 37) | 46.22 (± 47.901) | 49.78 (± 48.521) | 52.7 (± 46.015)  |
| Month 12 (n=35, 41, 40) | 53.58 (± 47.785) | 53.63 (± 48.358) | 58.03 (± 46.264) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Asthma Symptom Free Days

|  |  |
|--|--|
| End point title  | Percentage of Asthma Symptom Free Days |
| End point description:   |  |
| Days without Asthma Symptom documented in the participant's diary were reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point. |  |
| End point type   | Secondary                              |
| End point timeframe:   |  |
| Months 1, 2, 4, 6, 8, 10 and 12  |  |

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo          |
|--------------------------------------|--------------------|--------------------|------------------|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group  |
| Number of subjects analysed          | 79                 | 76                 | 84               |
| Units: percentage of days            |                    |                    |                  |
| arithmetic mean (standard deviation) |                    |                    |                  |
| Month 1 (n=62, 60, 60)               | 37.32 (± 40.983)   | 36.95 (± 42.207)   | 35 (± 43.032)    |
| Month 2 (n=61, 50, 56)               | 38.47 (± 44.743)   | 41.16 (± 44.738)   | 33.56 (± 44.161) |
| Month 4 (n=54, 55, 59)               | 42.57 (± 46.573)   | 38.83 (± 44.042)   | 35.78 (± 43.538) |
| Month 6 (n=53, 50, 51)               | 41.75 (± 46.474)   | 39.87 (± 43.744)   | 40.09 (± 45.274) |
| Month 8 (n=46, 46, 46)               | 38.86 (± 43.312)   | 43.9 (± 45.377)    | 40.03 (± 43.369) |
| Month 10 (n=43, 47, 44)              | 41 (± 46.575)      | 41.65 (± 47.435)   | 39.83 (± 44.332) |
| Month 12 (n=42, 44, 45)              | 43.2 (± 46.787)    | 42.03 (± 47.093)   | 44.61 (± 46.12)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Quality of Life Assessments as per Paediatric Asthma Quality of Life Questionnaire, Standardized (PAQLQ[S])

|                 |   |
|-----------------|---|
| End point title | Quality of Life Assessments as per Paediatric Asthma Quality of Life Questionnaire, Standardized (PAQLQ[S]) |
|-----------------|---|

End point description:

The PAQLQ(S) consists of 23 items divided into three domains: Activity limitations (items 1-3, 19, 22); Symptoms (items 4, 6, 8, 10, 12, 14, 16, 18, 20, 23) and Emotional function (items 5, 7, 9, 11, 13, 15, 17, 21). Participants were asked to answer each question using a seven-point scale (where "1" indicated maximum impairment and "7" indicated no impairment) and recall their experience during the previous week. Overall PAQLQ score is equal to the mean of all 23 items for a total possible score 1 (worst) to 7 (best). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

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

End point timeframe:

Months 2, 6 and 12

| End point values                     | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 79                 | 76                 | 84              |  |
| Units: score on a scale              |                    |                    |                 |  |
| arithmetic mean (standard deviation) |                    |                    |                 |  |
| Month 2 (n=70, 73, 75)               | 6.21 (± 0.979)     | 6.27 (± 0.878)     | 6.08 (± 1.031)  |  |
| Month 6 (n=65, 72, 72)               | 6.33 (± 0.874)     | 6.26 (± 0.982)     | 6.3 (± 0.933)   |  |
| Month 12 (n=64, 69, 65)              | 6.42 (± 0.786)     | 6.34 (± 0.946)     | 6.36 (± 0.824)  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Quality of Life Assessments as per Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)

|                 |   |
|-----------------|---|
| End point title | Quality of Life Assessments as per Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) |
|-----------------|---|

End point description:

The PACQLQ consists of 13 items divided into two domains: Activity limitations (items 2, 4, 6, 8) and Emotional function (items 1, 3, 5, 7, 9, 10, 11, 12, 13). Caregivers answered each question using a seven-point scale (whereby "1" indicated maximum impairment and "7" indicated no impairment) and recalled their experiences during the previous week. Overall PACQLQ score is equal to the mean of all 13

items for a total possible score of 1 (worst) to 7 (best). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Months 2, 6 and 12   |           |

| <b>End point values</b>              | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 79                    | 76                    | 84              |  |
| Units: score on a scale              |                       |                       |                 |  |
| arithmetic mean (standard deviation) |                       |                       |                 |  |
| Month 2 (n=73, 73, 76)               | 5.87 (± 1.196)        | 6.16 (± 1.033)        | 6.08 (± 1.078)  |  |
| Month 6 (n=67, 72, 73)               | 6.15 (± 1.005)        | 6.16 (± 1.115)        | 6.31 (± 0.927)  |  |
| Month 12 (n=66, 69, 66)              | 6.32 (± 0.849)        | 6.25 (± 0.712)        | 6.31 (± 0.899)  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Clinically Significant Vital Signs Findings

|   |   |
|---|---|
| End point title   | Number of Participants with Clinically Significant Vital Signs Findings |
| End point description:  |   |
| Vital signs included body temperature, systolic and diastolic blood pressure and heart rate in beats per minute (bpm). The investigator determined if the result was clinically significant based on the following criteria: Systolic Blood Pressure >130 mmHg or <80 mmHg or a >20 mmHg difference from Baseline; Diastolic Blood Pressure > 85 mmHg; and Resting Heart Rate >140 bpm or <60 bpm or a >30 bpm difference from Baseline. Safety analysis set included all randomized participants who received at least 1 dose of trial medication. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Up to 12 months   |   |

| <b>End point values</b>     | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 79                    | 76                    | 84              |  |
| Units: participants         | 0                     | 0                     | 0               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Clinically Significant Physical Examination Findings

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Clinically Significant Physical Examination Findings |
|-----------------|--|

End point description:

A thorough physical examination was performed consisting of examinations of the following body systems: (1) eyes; (2) ears, nose, throat; (3) lungs/thorax; (4) heart/cardiovascular system; (5) abdomen; (6) skin and mucosae; (7) nervous system; (8) lymph nodes; (9) musculo-skeletal system; (10) physical examinations other than body systems described in (1) to (9). The investigator determined if any of the findings were clinically significant. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

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

End point timeframe:

Up to 12 months

| End point values            | Ciclesonide 100 µg | Ciclesonide 200 µg | Placebo         |  |
|-----------------------------|--------------------|--------------------|-----------------|--|
| Subject group type          | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed | 79                 | 76                 | 84              |  |
| Units: participants         | 0                  | 0                  | 0               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Clinically Significant Laboratory Values

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Clinically Significant Laboratory Values |
|-----------------|--|

End point description:

Clinically significant laboratory values were hematology and chemistry tests determined by the investigator to be clinically significant based on the following criteria: Hemoglobin <9.5 g/dL; Erythrocytes <3.0 x 10<sup>6</sup>/µL or >6.5 x 10<sup>6</sup>/µL; White Blood Count <3000/mm<sup>3</sup> or >20000/mm<sup>3</sup>; serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), gamma-glutamyl transpeptidase (GGT), Total Bilirubin and Glucose >2 times Upper limit of Normal Range (ULNR); Alkaline Phosphatase and Creatine Kinase >3 times ULNR; Creatinine >1.5 times ULN; Potassium >5.0 mmol/L or <3.0 mmol/L; and Sodium >150 mmol/L or <130 mmol/L. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>     | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 79                    | 76                    | 84              |  |
| Units: participants         | 0                     | 0                     | 0               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Adverse Events and Serious Adverse Events

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Adverse Events and Serious Adverse Events |
|-----------------|---|

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A SAE is any untoward medical occurrence that at any dose results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in congenital anomaly/birth defect or any other important medical condition considered serious based on medical and scientific judgement. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

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

End point timeframe:

Up to 12 months

| <b>End point values</b>     | Ciclesonide 100<br>µg | Ciclesonide 200<br>µg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 79                    | 76                    | 84              |  |
| Units: participants         |                       |                       |                 |  |
| Adverse Events              | 61                    | 64                    | 63              |  |
| Serious Adverse Events      | 2                     | 2                     | 2               |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 months

Adverse event reporting additional description:

At each visit investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by participant or observed by investigator was recorded, irrespective of relation to treatment. All adverse events and serious adverse events were coded according to MedDRA versions 8.0, 8.1, 9.0 and 9.1.

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 9.1 |
|--------------------|-----|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Ciclesonide 100 µg |
|-----------------------|--------------------|

Reporting group description:

Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Ciclesonide 200 µg |
|-----------------------|--------------------|

Reporting group description:

Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

| <b>Serious adverse events</b>                     | Ciclesonide 100 µg | Placebo        | Ciclesonide 200 µg |
|---|--------------------|----------------|--------------------|
| Total subjects affected by serious adverse events |                    |                |                    |
| subjects affected / exposed                       | 2 / 79 (2.53%)     | 2 / 84 (2.38%) | 2 / 76 (2.63%)     |
| number of deaths (all causes)                     | 0                  | 0              | 0                  |
| number of deaths resulting from adverse events    | 0                  | 0              | 0                  |
| Surgical and medical procedures                   |                    |                |                    |
| Myringoplasty                                     |                    |                |                    |
| subjects affected / exposed                       | 0 / 79 (0.00%)     | 0 / 84 (0.00%) | 1 / 76 (1.32%)     |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 0          | 0 / 1              |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0          | 0 / 0              |
| Nervous system disorders                          |                    |                |                    |
| Headache  |                    |                |                    |
| subjects affected / exposed                       | 0 / 79 (0.00%)     | 1 / 84 (1.19%) | 0 / 76 (0.00%)     |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 1          | 0 / 0              |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0          | 0 / 0              |
| Ear and labyrinth disorders                       |                    |                |                    |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Vertigo   |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 84 (1.19%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Asthma  |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 84 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Epistaxis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 84 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Arthritis bacterial                             |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 1 / 84 (1.19%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Laryngitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 79 (0.00%) | 0 / 84 (0.00%) | 1 / 76 (1.32%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lobar pneumonia                                 |                |                |                |
| subjects affected / exposed                     | 1 / 79 (1.27%) | 0 / 84 (0.00%) | 0 / 76 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | Ciclesonide 100 µg | Placebo          | Ciclesonide 200 µg |
|---|--------------------|------------------|--------------------|
| Total subjects affected by non-serious adverse events |                    |                  |                    |
| subjects affected / exposed                           | 56 / 79 (70.89%)   | 56 / 84 (66.67%) | 55 / 76 (72.37%)   |
| Nervous system disorders                              |                    |                  |                    |

|   |                                     |                        |                        |
|---|-------------------------------------|------------------------|------------------------|
| Headache<br>subjects affected / exposed<br>occurrences (all)  | Additional description: non-serious |                        |                        |
|   | 4 / 79 (5.06%)<br>6                 | 8 / 84 (9.52%)<br>10   | 7 / 76 (9.21%)<br>10   |
| General disorders and administration site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 6 / 79 (7.59%)<br>6                 | 4 / 84 (4.76%)<br>5    | 2 / 76 (2.63%)<br>2    |
| Respiratory, thoracic and mediastinal disorders   | Additional description: non-serious |                        |                        |
| Asthma<br>subjects affected / exposed<br>occurrences (all)  | 35 / 79 (44.30%)<br>60              | 39 / 84 (46.43%)<br>82 | 38 / 76 (50.00%)<br>64 |
| Cough<br>subjects affected / exposed<br>occurrences (all)   | 6 / 79 (7.59%)<br>8                 | 6 / 84 (7.14%)<br>7    | 4 / 76 (5.26%)<br>10   |
| Rhinitis allergic<br>subjects affected / exposed<br>occurrences (all)   | 7 / 79 (8.86%)<br>7                 | 4 / 84 (4.76%)<br>6    | 4 / 76 (5.26%)<br>4    |
| Infections and infestations   |                                     |                        |                        |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)   | 5 / 79 (6.33%)<br>5                 | 2 / 84 (2.38%)<br>2    | 3 / 76 (3.95%)<br>4    |
| Influenza<br>subjects affected / exposed<br>occurrences (all)   | 3 / 79 (3.80%)<br>3                 | 3 / 84 (3.57%)<br>3    | 6 / 76 (7.89%)<br>8    |
| Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 79 (1.27%)<br>1                 | 1 / 84 (1.19%)<br>1    | 4 / 76 (5.26%)<br>4    |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 13 / 79 (16.46%)<br>20              | 14 / 84 (16.67%)<br>30 | 9 / 76 (11.84%)<br>18  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 5 / 79 (6.33%)<br>5                 | 4 / 84 (4.76%)<br>5    | 4 / 76 (5.26%)<br>5    |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)  | 4 / 79 (5.06%)<br>4                 | 3 / 84 (3.57%)<br>5    | 0 / 76 (0.00%)<br>0    |

|                                   |                  |                  |                  |
|-----------------------------------|------------------|------------------|------------------|
| Sinusitis                         |                  |                  |                  |
| subjects affected / exposed       | 1 / 79 (1.27%)   | 5 / 84 (5.95%)   | 1 / 76 (1.32%)   |
| occurrences (all)                 | 2                | 7                | 1                |
| Upper respiratory tract infection |                  |                  |                  |
| subjects affected / exposed       | 18 / 79 (22.78%) | 16 / 84 (19.05%) | 19 / 76 (25.00%) |
| occurrences (all)                 | 28               | 35               | 31               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 09 September 2004 | Amendment 1: • Addition of history of cataracts and/or glaucoma as an exclusion criterion due to the potential class effect of ocular disturbances with the long-term use of inhaled corticosteroid (ICS).   |
| 01 November 2004  | Amendment 2: • Removal of the hyper-responsiveness test (challenge test) as a pre-randomisation requirement for study inclusion, • Dose for fluticasone propionate (FP) to be consistent with the marketed dosing of Flovent® and the standard in treatment (two puffs of 125 µg FP per day). • Inclusion of a guideline on inhalation technique for study medication that accommodated the full potential age range of participants enrolled in the trial. • Amendment of the paradigm for treatment of exacerbations to add a guideline on how to treat a participant who is getting better within 24 hours with regard to usage of FP. • Amendment of the study time table. |
| 08 August 2005    | Amendment 3: • Administrative change in personnel and contact information. • Changes referring to the use of intranasal medications for the treatment of rhinitis. • Exclusion criterion concerning use of topical steroids was originally implemented to limit any confounding variable. However, according to the literature available currently, no impact on growth or HPA axis has been demonstrated in many studies of topical nasal steroids.   |
| 10 March 2006     | Amendment 4: Administrative changes to study personnel and contact information; submission to authorities; study protocol, documentation and archiving of data, and an increase in the number of study sites, reflecting the expansion of the trial to additional sites in countries other than Canada (Brazil and South Africa).  |
| 22 June 2007      | Amendment 5: Administrative changes in the local sponsor and contact information reflecting a change in country of origin for study sites (from Canada, Brazil and South Africa to Canada, Hungary and South Africa). Change in study timelines.   |
| 17 January 2008   | Amendment 6: Administrative changes to study timelines and local sponsor name and contact information.   |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported