# Clinical trial results:
# Control of moderate or severe asthma with 160, 320 and 640 mcg ciclesonide/day. A one-year randomised, double-blind, multicenter trial.

## Summary

| | |
|---|---|
| EudraCT number | 2011-000683-99 |
| Trial protocol | DE |
| Global end of trial date | 15 August 2014 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 11 August 2016 |
| First version publication date | 10 May 2016 |
| Version creation reason | • New data added to full data set<br>Harmonization |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CL-9709-301-RD |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | U1111-1133-6333 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 61 Aldwych, London, United Kingdom, WC2B 4AE |
| Public contact | Program Manager, Takeda Development Centre Europe Ltd., +1 877-825-3327, clinicaltrialregistry@tpna.com |
| Scientific contact | Program Manager, Takeda Development Centre Europe Ltd., +1 877-825-3327, clinicaltrialregistry@tpna.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 22 May 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 August 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 August 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The aim of the trial is to investigate asthma control with 160 to 640 mcg ciclesonide/day. Asthma control will be assessed by the Asthma Control Questionnaire (ACQ).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 November 2011 |
| 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 | Brazil: 86 |
| Country: Number of subjects enrolled | Argentina: 72 |
| Country: Number of subjects enrolled | Germany: 60 |
| Country: Number of subjects enrolled | Israel: 59 |
| Country: Number of subjects enrolled | Russian Federation: 90 |
| Worldwide total number of subjects | 367 |
| EEA total number of subjects | 60 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 16 |
| Adults (18-64 years) | 314 |
| From 65 to 84 years | 37 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects took part in the study at 5 investigative sites in Argentina, Brazil, Germany, Israel and Russia from 10 November 2011 to 15 August 2014.

### Pre-assignment

Screening details:

Subjects with a historical diagnosis of persistent bronchial asthma for at least 6 months,treated with a stable inhaled corticosteroid (ICS)dose for at least 12 weeks were enrolled in a single-blind baseline period receiving 160 microgram(mcg)ciclesonide,then a double-blind treatment period in 1 of 3 treatment arms: ciclesonide 160,320,640 mcg.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Treatment Period: Ciclesonide 160 mcg |

Arm description:

Ciclesonide 80 mcg, metered dose inhaler (MDI), inhalational, twice daily for up to 3 weeks in the baseline period. Ciclesonide 80 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ciclesonide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Ciclesonide 80 mcg, metered dose inhaler (MDI), inhalational, twice daily for up to 3 weeks in the baseline period. Ciclesonide 80 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| **Arm title** | Treatment Period: Ciclesonide 320 mcg |

Arm description:

Ciclesonide 160 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ciclesonide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Ciclesonide 160 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| **Arm title** | Treatment Period: Ciclesonide 640 mcg |

Arm description:

Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment

period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ciclesonide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| **Number of subjects in period 1** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg |
|---|---|---|---|
| Started | 120 | 122 | 125 |
| Completed | 89 | 92 | 97 |
| Not completed | 31 | 30 | 28 |
| Consent withdrawn by subject | 16 | 12 | 9 |
| Adverse event, non-fatal | 1 | 1 | 3 |
| Pregnancy | 1 | 1 | - |
| Miscellaneous | 5 | 1 | 4 |
| Discontinuation criterion fulfilled | 2 | - | 2 |
| Lost to follow-up | - | 1 | 1 |
| Deterioration in asthma | 6 | 14 | 9 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Treatment Period: Ciclesonide 160 mcg |
| Reporting group description: | |
| Ciclesonide 80 mcg, metered dose inhaler (MDI), inhalational, twice daily for up to 3 weeks in the baseline period. Ciclesonide 80 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |
| Reporting group title | Treatment Period: Ciclesonide 320 mcg |
| Reporting group description: | |
| Ciclesonide 160 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |
| Reporting group title | Treatment Period: Ciclesonide 640 mcg |
| Reporting group description: | |
| Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |

| Reporting group values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg |
|---|---|---|---|
| Number of subjects | 120 | 122 | 125 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 43.2 | 44.7 | 45.3 |
| standard deviation | ± 14.86 | ± 15.6 | ± 16.22 |
| Gender, Male/Female | | | |
| Units: subjects | | | |
| Female | 72 | 77 | 81 |
| Male | 48 | 45 | 44 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Black or African American | 6 | 5 | 4 |
| White | 113 | 115 | 114 |
| Unknown or Not Reported | 1 | 2 | 7 |
| History of exacerbations | | | |
| Asthma exacerbations were defined as a worsening of asthma requiring either treatment with oral (or other systemic) glucocorticosteroids for at least 3 days or hospitalisation or a visit to the emergency room because of asthma. | | | |
| Units: Subjects | | | |
| 0x | 70 | 70 | 63 |
| 1x | 17 | 19 | 21 |
| 2-3 | 4 | 3 | 4 |
| 4+ | 0 | 0 | 0 |
| Unknown | 29 | 30 | 37 |
| Smoking Status | | | |
| Units: Subjects | | | |
| Never | 109 | 102 | 109 |
| Current | 1 | 1 | 1 |
| Former | 10 | 19 | 15 |

| | | | |
|---|---|---|---|
| Prestudy ICS dose<br>Units: Subjects | | | |
| <200(mcg/day) fluticasone propionate(FP)equivalent | 3 | 3 | 2 |
| Low: ≥200 mcg/day (≤) 250 mcg/day FP equivalent | 40 | 37 | 42 |
| Medium:>250 mcg/day to ≤500 mcg/day FP equivalent | 72 | 75 | 70 |
| High:>500 mcg/day to ≤1000 mcg/day FP equivalent | 5 | 7 | 11 |
| Height<br>Units: meter (m) | | | |
| arithmetic mean | 1.65 | 1.66 | 1.65 |
| standard deviation | ± 0.093 | ± 0.101 | ± 0.104 |
| Weight<br>Units: kilograms (kg) | | | |
| arithmetic mean | 74.59 | 77.98 | 73.72 |
| standard deviation | ± 16.371 | ± 18.993 | ± 14.66 |
| Body Mass Index<br>Units: kilogram per meter square (kg/m2) | | | |
| arithmetic mean | 27.34 | 28.42 | 27.12 |
| standard deviation | ± 5.217 | ± 6.346 | ± 5.373 |
| Baseline asthma control questionnaire (ACQ) | | | |
| ACQ=5 questions about symptoms,1 question about beta 2-agonist use and 1 about lung function (FEV1% predicted).Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale.The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. | | | |
| Units: units on scale | | | |
| arithmetic mean | 2.24 | 2.16 | 2.2 |
| standard deviation | ± 0.304 | ± 0.384 | ± 0.361 |
| Pre-forced expiratory volume in 1 second (FEV1) | | | |
| Pre-FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration prior to salbutamol administration. | | | |
| Units: liter (L) | | | |
| arithmetic mean | 2.2 | 2.35 | 2.23 |
| standard deviation | ± 0.792 | ± 0.798 | ± 0.801 |
| Post-FEV1 | | | |
| Post-FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration after salbutamol administration. | | | |
| Units: Lx | | | |
| arithmetic mean | 2.71 | 2.84 | 2.76 |
| standard deviation | ± 0.915 | ± 0.883 | ± 0.906 |
| FEV1 reversibility | | | |
| Reversibility is assessed using FEV1 measurements. Percent reversibility is calculated as the difference between highest FEV1 after salbutamol and highest FEV 1 before salbutamol divided by highest FEV 1 before salbutamol. FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. | | | |
| Units: Lx | | | |
| arithmetic mean | 25.5 | 23 | 26.5 |
| standard deviation | ± 17.02 | ± 17.1 | ± 20.78 |
| Pre FEV1 predicted | | | |
| Pre-FEV1 is the maximal predicted volume of air exhaled in the first second of a forced expiration from a | | | |

| | | | |
|---|---|---|---|
| position of full inspiration prior to salbutamol administration calculated according to the respective formula for different age groups of subjects. | | | |
| Units: Lx | | | |
| arithmetic mean | 69.095 | 74.345 | 71.835 |
| standard deviation | ± 18.4683 | ± 16.7285 | ± 18.4365 |
| Post FEV1 predicted | | | |
| Post-FEV1 is the maximal predicted volume of air exhaled in the first second of a forced expiration from a position of full inspiration after salbutamol administration calculated according to the respective formula for different age groups of subjects. | | | |
| Units: Lx | | | |
| arithmetic mean | 84.893 | 90.168 | 88.505 |
| standard deviation | ± 19.3038 | ± 17.7365 | ± 17.7105 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 367 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender, Male/Female | | | |
| Units: subjects | | | |
| Female | 230 | | |
| Male | 137 | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Black or African American | 15 | | |
| White | 342 | | |
| Unknown or Not Reported | 10 | | |
| History of exacerbations | | | |
| Asthma exacerbations were defined as a worsening of asthma requiring either treatment with oral (or other systemic) glucocorticosteroids for at least 3 days or hospitalisation or a visit to the emergency room because of asthma. | | | |
| Units: Subjects | | | |
| 0x | 203 | | |
| 1x | 57 | | |
| 2-3 | 11 | | |
| 4+ | 0 | | |
| Unknown | 96 | | |
| Smoking Status | | | |
| Units: Subjects | | | |
| Never | 320 | | |
| Current | 3 | | |
| Former | 44 | | |
| Prestudy ICS dose | | | |
| Units: Subjects | | | |
| <200(mcg/day) fluticasone propionate(FP)equivalent | 8 | | |
| Low: ≥200 mcg/day (≤) 250 mcg/day FP equivalent | 119 | | |
| Medium:>250 mcg/day to ≤500 mcg/day FP equivalent | 217 | | |

| | | | |
|---|---|---|---|
| High:>500 mcg/day to ≤1000 mcg/day FP equivalent | 23 | | |

| | | | |
|---|---|---|---|
| Height<br>Units: meter (m)<br>arithmetic mean<br>standard deviation | - | | |
| Weight<br>Units: kilograms (kg)<br>arithmetic mean<br>standard deviation | - | | |
| Body Mass Index<br>Units: kilogram per meter square (kg/m2)<br>arithmetic mean<br>standard deviation | - | | |
| Baseline asthma control questionnaire (ACQ) | | | |
| ACQ=5 questions about symptoms,1 question about beta 2-agonist use and 1 about lung function (FEV1% predicted).Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale.The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. | | | |
| Units: units on scale<br>arithmetic mean<br>standard deviation | - | | |
| Pre-forced expiratory volume in 1 second (FEV1) | | | |
| Pre-FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration prior to salbutamol administration. | | | |
| Units: liter (L)<br>arithmetic mean<br>standard deviation | - | | |
| Post-FEV1 | | | |
| Post-FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration after salbutamol administration. | | | |
| Units: Lx<br>arithmetic mean<br>standard deviation | - | | |
| FEV1 reversibility | | | |
| Reversibility is assessed using FEV1 measurements. Percent reversibility is calculated as the difference between highest FEV1 after salbutamol and highest FEV 1 before salbutamol divided by highest FEV 1 before salbutamol. FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. | | | |
| Units: Lx<br>arithmetic mean<br>standard deviation | - | | |
| Pre FEV1 predicted | | | |
| Pre-FEV1 is the maximal predicted volume of air exhaled in the first second of a forced expiration from a position of full inspiration prior to salbutamol administration calculated according to the respective formula for different age groups of subjects. | | | |
| Units: Lx<br>arithmetic mean<br>standard deviation | - | | |
| Post FEV1 predicted | | | |

| Post-FEV1 is the maximal predicted volume of air exhaled in the first second of a forced expiration from a position of full inspiration after salbutamol administration calculated according to the respective formula for different age groups of subjects. | | | |
|---|---|---|---|
| Units: Lx | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Treatment Period: Ciclesonide 160 mcg |
| Reporting group description: | |
| Ciclesonide 80 mcg, metered dose inhaler (MDI), inhalational, twice daily for up to 3 weeks in the baseline period. Ciclesonide 80 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |
| Reporting group title | Treatment Period: Ciclesonide 320 mcg |
| Reporting group description: | |
| Ciclesonide 160 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |
| Reporting group title | Treatment Period: Ciclesonide 640 mcg |
| Reporting group description: | |
| Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |
| Subject analysis set title | Treatment Periods: Ciclesonide 640 mcg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period. | |

### Primary: Asthma Control Questionnaire (ACQ) Score at Baseline

| | |
|---|---|
| End point title | Asthma Control Questionnaire (ACQ) Score at Baseline[1] |
| End point description: | |
| The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The intent-to-treat (ITT) analysis set included subjects having at least 1 postrandomization efficacy assessment. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline | |

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: Only descriptive data was planned to be reported for this endpoint.

| End point values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 119 | 122 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard error) | 2.24 (± 0.031) | 2.15 (± 0.035) | 2.19 (± 0.032) | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in ACQ Score to Tlast

| End point title | Change from Baseline in ACQ Score to Tlast |
|---|---|

End point description:

The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Week 52

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 119 | 122 | |
| Units: units on a scale | | | | |
| arithmetic mean (standard error) | -0.833 (± 0.1028) | -0.799 (± 0.1019) | -0.955 (± 0.0969) | |

### Statistical analyses

| **Statistical analysis title** | Ciclesonide 160 mcg vs Ciclesonide 640 mcg |
|---|---|

Statistical analysis description:

Least square (LS) mean difference were derived from an ANCOVA model with baseline ACQ and age as covariates, and treatment, centre pool, sex, and prestudy ICS dose as factors.

| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
|---|---|
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2988 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.122 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.353 |
| upper limit | 0.109 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1175 |

| **Statistical analysis title** | Ciclesonide 160 mcg vs Ciclesonide 320 mcg |
|---|---|
| Statistical analysis description: | |
| LS mean difference were derived from an ANCOVA model with baseline ACQ and age as covariates, and treatment, centre pool, sex, and prestudy ICS dose as factors. | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7741 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.034 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.198 |
| upper limit | 0.266 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.118 |

| **Statistical analysis title** | Ciclesonide 320 mcg vs Ciclesonide 640 mcg |
|---|---|
| Statistical analysis description: | |
| LS mean difference were derived from an ANCOVA model with baseline ACQ and age as covariates, and treatment, centre pool, sex, and prestudy ICS dose as factors. | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 241 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1835 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.156 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.387 |
| upper limit | 0.074 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1172 |

| **Secondary: Time Course of ACQ** | |
|---|---|
| End point title | Time Course of ACQ |

End point description:

Time course of incidence of 0.5 points improvement of ACQ score was evaluated.Mean ACQ values over time by treatment group for on-treatment site measurements assessed. It was done on a weekly base using home-based and site-based ACQ measurements. ACQ=5 questions about symptoms,1 question about beta 2-agonist use and 1 about lung function (FEV1% predicted).Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale.The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma". The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Baseline, Week 52 (Treatment period)

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 105 | 108 | 115 | |
| Units: Weeks | | | | |
| median (full range (min-max)) | 1.1 (0 to 4.4) | 1 (0 to 3.9) | 1 (0 to 4.6) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Well-Controlled Asthma Over the Course of the Study

| End point title | Time to Well-Controlled Asthma Over the Course of the Study |
|---|---|

End point description:

The time to well-controlled asthma was defined as the number of weeks from randomization to the first instance with an ACQ score of 0.75 or lower. The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The intent-to-treat ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Baseline up to Week 52 (treatment period)

| End point values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 119 | 122 | |
| Units: weeks | | | | |
| number (not applicable) | 1211 | 1514 | 1447 | |

**Statistical analyses**

| Statistical analysis title | Ciclesonide 160 mcg vs Ciclesonide 640 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4175 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Hodges-Lehmann point estimate |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 5 |

| Statistical analysis title | Ciclesonide 160 mcg vs Ciclesonide 320 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8465 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Hodges-Lehmann point estimate |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 4 |

**Secondary: Number of Subjects With Well-controlled Asthma and ACQ Improvement at the End of the Study**

| End point title | Number of Subjects With Well-controlled Asthma and ACQ |
|---|---|

| | |
|---|---|
| | Improvement at the End of the Study |

End point description:

Well-controlled asthma at the end of the study was defined as a subjects with an ACQ score of 0.75 or lower. The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The intent-to-treat ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Week 52

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 122 | 125 | |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Well-controlled Asthma | 38 | 45 | 51 | |
| ACQ Improvement | 87 | 81 | 85 | |

## Statistical analyses

| **Statistical analysis title** | Wellcontrolled Asthma Ciclesonide 160mcgvs320mcg |
|---|---|

Statistical analysis description:

Well-controlled Asthma

| | |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4186 |
| Method | Fisher exact |

| **Statistical analysis title** | Wellcontrolled Asthma Ciclesonide 160mcgvs640mcg |
|---|---|

Statistical analysis description:

Well-controlled Asthma

| | |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |

| | |
|---|---|
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.146 |
| Method | Fisher exact |

| **Statistical analysis title** | Wellcontrolled Asthma Ciclesonide 320mcgvs640mcg |
|---|---|
| Statistical analysis description:<br>Well-controlled Asthma | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6017 |
| Method | Fisher exact |

| **Statistical analysis title** | ACQ Improvement  Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description:<br>ACQ Improvement | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3305 |
| Method | Fisher exact |

| **Statistical analysis title** | ACQ Improvement Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ Improvement | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.486 |
| Method | Fisher exact |

| **Statistical analysis title** | ACQ Improvement Ciclesonide 320 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ Improvement | |

| | |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8922 |
| Method | Fisher exact |

## Secondary: Number of Subjects Reporting Time to First Well-Controlled Asthma and ACQ Improvement

| | |
|---|---|
| End point title | Number of Subjects Reporting Time to First Well-Controlled Asthma and ACQ Improvement |

End point description:

Well-controlled asthma at the end of the study was defined as a subjects with an ACQ score of 0.75 or lower.The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Baseline up to Week 52 (treatment period)

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 122 | 125 | |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Well-controlled Asthma | 73 | 84 | 81 | |
| ACQ Improvement | 112 | 107 | 115 | |

### Statistical analyses

| **Statistical analysis title** | Well-controlled Asthma Ciclesonide 160mcgvs640 mcg |
|---|---|

Statistical analysis description:

Well-controlled Asthma

| | |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |

| | |
|---|---|
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6062 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.042 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.221 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0806 |

| **Statistical analysis title** | ACQ Improvement Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ Improvement | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4674 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.921 |
| upper limit | 1.197 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0669 |

| **Statistical analysis title** | Well-controlled Asthma Ciclesonide 160mcgvs320 mcg |
|---|---|
| Statistical analysis description: | |
| Well-controlled Asthma | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2523 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.201 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.878 |
| upper limit | 1.642 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1597 |

| **Statistical analysis title** | ACQ Improvement Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ Improvement | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5026 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.913 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 1.191 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1354 |

| **Statistical analysis title** | Well-controlled Asthma Ciclesonide 320mcgvs640 mcg |
|---|---|
| Statistical analysis description: | |
| Well-controlled Asthma | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4893 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.898 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.661 |
| upper limit | 1.219 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.156 |

| **Statistical analysis title** | ACQ Improvement Ciclesonide 320 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ Improvement | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2193 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.181 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.906 |
| upper limit | 1.538 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1351 |

## Secondary: Number of Subjects Reporting Time to First Well-Controlled Asthma Measurement by ACQ Cut-Off Point

| End point title | Number of Subjects Reporting Time to First Well-Controlled Asthma Measurement by ACQ Cut-Off Point |
|---|---|

End point description:

Well-controlled asthma was defined as an ACQ score of equal to or lower than the ACQ cut-off point.The ACQ was developed to measure the adequacy of asthma control in clinical research and in clinical practice. It includes 5 questions about symptoms, 1 question about beta 2 -agonist use and 1 about lung function (FEV1% predicted). Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale. The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0 (well controlled) and 6 (extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and < 1.5 indicate partly controlled asthma, and a score >= 1.5 indicates uncontrolled asthma. The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Baseline up to Week 52 (treatment period)

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 122 | 125 | |
| Units: subjects | | | | |
| number (not applicable) | | | | |

| | | | | |
|---|---|---|---|---|
| ACQ cut-off at 0.5 | 56 | 69 | 63 | |
| ACQ cut-off at 1.0 | 91 | 95 | 93 | |
| ACQ cut-off at 1.25 | 99 | 101 | 101 | |
| ACQ cut-off at 1.5 | 103 | 105 | 107 | |

**Statistical analyses**

| **Statistical analysis title** | ACQ cut-off at 0.5 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 0.5 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5397 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.058 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.884 |
| upper limit | 1.266 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0917 |

| **Statistical analysis title** | ACQ cut-off at 1.0 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 1.0 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9458 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.005 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.87 |
| upper limit | 1.161 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0738 |

| **Statistical analysis title** | ACQ cut-off at 1.25 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 1.25 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7213 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.026 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.893 |
| upper limit | 1.178 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0708 |

| **Statistical analysis title** | ACQ cut-off at 1.5 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 1.5 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4807 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.917 |
| upper limit | 1.202 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0692 |

| **Statistical analysis title** | ACQ cut-off at 0.5 Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 0.5 | |

| | |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.115 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.326 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.934 |
| upper limit | 1.884 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1791 |

| **Statistical analysis title** | ACQ cut-off at 1.0 Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 1.0 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6281 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.074 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.805 |
| upper limit | 1.431 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1467 |

| **Statistical analysis title** | ACQ cut-off at 1.25 Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 1.25 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |

| | |
|---|---|
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6853 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.059 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.803 |
| upper limit | 1.397 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1415 |

| **Statistical analysis title** | ACQ cut-off at 1.5 Ciclesonide 160 mcg vs 320 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 1.5 | |
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6995 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.055 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.804 |
| upper limit | 1.385 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1388 |

| **Statistical analysis title** | ACQ cut-off at 0.5 Ciclesonide 320 mcg vs 640 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 0.5 | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.308 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.837 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.595 |
| upper limit | 1.178 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1744 |

| **Statistical analysis title** | ACQ cut-off at 1.0 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 1.0 | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6645 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.939 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.705 |
| upper limit | 1.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1461 |

| **Statistical analysis title** | ACQ cut-off at 1.25 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description: | |
| ACQ cut-off at 1.25 | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9564 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.992 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.753 |
| upper limit | 1.308 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1408 |

| **Statistical analysis title** | ACQ cut-off at 1.5 Ciclesonide 160 mcg vs 640 mcg |
|---|---|
| Statistical analysis description:<br>ACQ cut-off at 1.5 | |
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7367 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.047 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1.371 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1375 |

| **Secondary: Number of Subjects Reporting Time to First Asthma Exacerbation** | |
|---|---|
| End point title | Number of Subjects Reporting Time to First Asthma Exacerbation |
| End point description:<br>Asthma exacerbations were defined as a worsening of asthma requiring either treatment with oral (or other systemic) glucocorticosteroids for at least 3 days or hospitalisation or a visit to the emergency room because of asthma. Baseline was defined as the average of the ACQ measurements of the last 2 weeks at site prior to first intake of double-blind study medication. The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment. | |
| End point type | Secondary |
| End point timeframe:<br>Baseline up to Week 52 (treatment period) | |

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 122 | 125 | |
| Units: subjects | | | | |
| number (not applicable) | 5 | 11 | 10 | |

**Statistical analyses**

| **Statistical analysis title** | Ciclesonide 160 mcg vs Ciclesonide 640 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2264 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.367 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.824 |
| upper limit | 2.267 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.2583 |

| **Statistical analysis title** | Ciclesonide 320 mcg vs Ciclesonide 640 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 320 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 247 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7732 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.882 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.375 |
| upper limit | 2.074 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4365 |

| **Statistical analysis title** | Ciclesonide 160 mcg vs Ciclesonide 320 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1373 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 2.102 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.789 |
| upper limit | 5.602 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.5001 |

## Secondary: Number of Subjects Reporting Asthma Exacerbations Rates

| | |
|---|---|
| End point title | Number of Subjects Reporting Asthma Exacerbations Rates |

End point description:

Subjects with at least 1 asthma exacerbation in the double-blind treatment period have been reported. As predefined in the protocol, the results for subjects with missing data for any category were not included. The ITT analysis set included subjects having at least 1 postrandomization efficacy assessment.

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

End point timeframe:

Baseline up to Week 52 (treatment period)

| End point values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 120 | 122 | 122 | |
| Units: subjects | | | | |
| number (not applicable) | 5 | 10 | 10 | |

### Statistical analyses

| Statistical analysis title | Ciclesonide 160 mcg vs Ciclesonide 320 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 640 mcg |
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.288 |
| Method | Fisher exact |

| Statistical analysis title | Ciclesonide 160 mcg vs Ciclesonide 640 mcg |
|---|---|
| Comparison groups | Treatment Period: Ciclesonide 160 mcg v Treatment Period: Ciclesonide 320 mcg |

| | |
|---|---|
| Number of subjects included in analysis | 242 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2864 |
| Method | Fisher exact |

## Secondary: Number of Subjects With Markedly High Benefits.

| | |
|---|---|
| End point title | Number of Subjects With Markedly High Benefits.[2] |

End point description:

Analyses was intended to identify subject subsets that would benefit from dose escalation.Analysis tested the potential factors, including age,sex,pretrial inhaled corticosteroid(ICS) dose category,history of exacerbations,baseline ACQ score,baseline BMI category and smoking status.ACQ=5 questions about symptoms,1 question about beta 2-agonist use and 1 about lung function (FEV1% predicted).Subjects recall their experiences during the previous 7 days and respond to each question using a 7-point scale.The items are equally weighted and the ACQ score is the mean of 7 items and ranges between 0(well controlled) and 6(extremely poorly controlled). Mean scores of =<0.75 indicate well-controlled asthma, scores between 0.76 and <1.5 indicate partly controlled asthma, and a score >=1.5 indicates uncontrolled asthma. SAS included all subjects who took at least 1 dose of study medication.One subjects erroneously randomized into 160 mcg arm actually received 640 mcg dose.

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

End point timeframe:

Week 1 up to Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for Ciclesonide 640 mcg arm has been reported as subject analysis set created additionally for this endpoint in order to report the 1 subject who was erroneously randomized into this treatment arm.

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Periods: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 119 | 122 | 126 | |
| Units: subjects | | | | |
| number (not applicable) | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Reporting One or More Treatment-emergent Adverse Events (TEAE)

| | |
|---|---|
| End point title | Number of Subjects Reporting One or More Treatment-emergent Adverse Events (TEAE)[3] |

End point description:

An Adverse Event(AE) is defined as any untoward medical occurrence in a clinical investigation subject administered a drug; it does not necessarily have to have a causal relationship with this treatment. AE can therefore be any unfavorable and unintended sign (eg, a clinically significant abnormal laboratory finding),symptom,or disease temporally associated with the use of a drug,whether or not it is considered related to the drug. TEAE is defined as an adverse event with an onset that occurs after receiving study drug. AEs included both serious AEs and non-serious AEs. Baseline of double-blind treatment period was

defined as the average of the measurements of the last 2 weeks at site prior to first intake of double-blind study medication. SAS included all subjects who took at least 1 dose of study medication. One subject erroneously randomized into 160 mcg arm, actually received 640 mcg dose. For safety analysis, subjects were analyzed based on the treatment they actually received.

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

End point timeframe:

Baseline period (Week -3 up to -1), treatment period (Baseline up to Week 56)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for Ciclesonide 640 mcg arm has been reported as subject analysis set created additionally for this endpoint in order to report the 1 subject who was erroneously randomized into this treatment arm.

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Periods: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 119 | 122 | 126 | |
| Units: subjects | | | | |
| number (not applicable) | 85 | 86 | 89 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Reporting Clinically Significant Change from Baseline in Vital Signs

| End point title | Number of Subjects Reporting Clinically Significant Change from Baseline in Vital Signs[4] |
|---|---|

End point description:

Vital signs included body temperature, blood pressure (BP) and pulse rate. Normal range for vital signs included: Systolic BP >170 millimeters of mercury (mm Hg) or <85 mm Hg, Diastolic BP >105 mm Hg, resting pulse rate: >120 bpm or <50 bpm, difference in systolic BP at Visit x (increase or decrease) compared with pretreatment >40 mm Hg and difference in pulse rate at Visit x (increase or decrease) compared with pretreatment >30 bpm. Baseline of double-blind treatment period was defined as the average of the measurements of the last 2 weeks at site prior to first intake of double-blind study medication. Safety analysis set included all subjects who took at least 1 dose of study medication. One subject erroneously randomized into 160 mcg arm, actually received 640 mcg dose. For safety analysis, subjects were analyzed based on the treatment they actually received.

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

End point timeframe:

Baseline period (Week -3 up to -1), treatment period (Baseline up to Week 56)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for Ciclesonide 640 mcg arm has been reported as subject analysis set created additionally for this endpoint in order to report the 1 subject who was erroneously randomized into this treatment arm.

| End point values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Periods: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 119 | 122 | 126 | |
| Units: subjects | | | | |
| number (not applicable) | 0 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Reporting Clinically Significant Change from Baseline in Physical Examination Findings

| End point title | Number of Subjects Reporting Clinically Significant Change from Baseline in Physical Examination Findings[5] |
|---|---|

End point description:

Physical examination consists of examinations of the following body systems: (1) eyes; (2) ears, nose, throat; (3) cardiovascular system; (4) respiratory system; (5) gastrointestinal system; (6) dermatologic system; (7) extremities; (8) musculoskeletal system; (9) nervous system; (10) lymph nodes; and (11) physical examinations other than body systems described in (1) to (10). Baseline of double-blind treatment period was defined as the average of the measurements of the last 2 weeks at site prior to first intake of double-blind study medication. Safety analysis set included all subject who took at least 1 dose of study medication. One subject erroneously randomized into 160 mcg arm, actually received 640 mcg dose. For safety analysis, subjects were analyzed based on the treatment they actually received.

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

End point timeframe:

Baseline period (Week -3 up to -1), treatment period (Baseline up to Week 56)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for Ciclesonide 640 mcg arm has been reported as subject analysis set created additionally for this endpoint in order to report the 1 subject who was erroneously randomized into this treatment arm.

| End point values | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Periods: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 119 | 122 | 126 | |
| Units: subjects | | | | |
| number (not applicable) | 0 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Markedly Abnormal Laboratory Values

| End point title | Number of Subjects With Markedly Abnormal Laboratory |
|---|---|

End point description:

The number of subjects with any markedly abnormal standard safety laboratory values collected throughout study. Baseline of double-blind treatment period was defined as the average of the measurements of the last 2 weeks at site prior to first intake of double-blind study medication. Safety analysis set included all subjects who took at least 1 dose of study medication. One subject erroneously randomized into 160 mcg arm, actually received 640 mcg dose. For safety analysis, subjects were analyzed based on the treatment they actually received.

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

End point timeframe:

Baseline period (Week -3 up to -1), treatment period (Baseline up to Week 56)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for Ciclesonide 640 mcg arm has been reported as subject analysis set created additionally for this endpoint in order to report the 1 subject who was erroneously randomized into this treatment arm.

| **End point values** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Periods: Ciclesonide 640 mcg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 119 | 122 | 126 | |
| Units: subjects | | | | |
| number (not applicable) | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are adverse events that started after the first dose of double-blind study drug and no more than 30 days for a serious adverse event after the last dose of double-blind study drug.

Adverse event reporting additional description:

Investigator documented any AEs and abnormal laboratory findings.Any event spontaneously reported was recorded,irrespective of the relation to study treatment. 1 subject erroneously randomized into 160 mcg arm,actually received 640 mcg dose.For safety analysis,subjects were analyzed based on the treatment they actually received.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Treatment Period: Ciclesonide 160 mcg |

Reporting group description:

Ciclesonide 80 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| Reporting group title | Treatment Period: Ciclesonide 320 mcg |

Reporting group description:

Ciclesonide 160 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| | |
|---|---|
| Reporting group title | Treatment Period: Ciclesonide 640 mcg |

Reporting group description:

Ciclesonide 320 mcg, MDI, inhalational, twice daily for up to 52 weeks in the double blind treatment period.

| Serious adverse events | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 9 / 122 (7.38%) | 0 / 126 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 122 (0.00%) | 0 / 126 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 122 (0.82%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |
| Nervous system disorders | | | |
| Cerebellar ischaemia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 122 (0.00%) | 0 / 126 (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 |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 122 (0.00%) | 0 / 126 (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 |
| Gastrointestinal disorders | | | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 failure | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 122 (0.00%) | 0 / 126 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Invertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 122 (0.00%) | 0 / 126 (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 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 122 (1.64%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 122 (0.82%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |
| Pulmonary tuberculosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 122 (0.82%) | 0 / 126 (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 |

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

| **Non-serious adverse events** | Treatment Period: Ciclesonide 160 mcg | Treatment Period: Ciclesonide 320 mcg | Treatment Period: Ciclesonide 640 mcg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 65 / 119 (54.62%) | 65 / 122 (53.28%) | 70 / 126 (55.56%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 22 / 119 (18.49%) | 23 / 122 (18.85%) | 16 / 126 (12.70%) |
| occurrences (all) | 67 | 82 | 58 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 7 / 122 (5.74%) | 4 / 126 (3.17%) |
| occurrences (all) | 5 | 9 | 5 |
| Cough | | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 7 / 122 (5.74%) | 3 / 126 (2.38%) |
| occurrences (all) | 6 | 15 | 3 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 8 / 119 (6.72%) | 3 / 122 (2.46%) | 6 / 126 (4.76%) |
| occurrences (all) | 10 | 4 | 8 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 2 / 122 (1.64%) | 8 / 126 (6.35%) |
| occurrences (all) | 7 | 5 | 14 |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 6 / 119 (5.04%) | 6 / 122 (4.92%) | 11 / 126 (8.73%) |
| occurrences (all) | 6 | 7 | 12 |
| Bronchitis | | | |
| subjects affected / exposed | 18 / 119 (15.13%) | 16 / 122 (13.11%) | 16 / 126 (12.70%) |
| occurrences (all) | 22 | 21 | 18 |
| Nasopharyngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 119 (19.33%) | 25 / 122 (20.49%) | 22 / 126 (17.46%) |
| occurrences (all) | 31 | 32 | 37 |
| Pharyngitis | | | |
| subjects affected / exposed | 4 / 119 (3.36%) | 8 / 122 (6.56%) | 4 / 126 (3.17%) |
| occurrences (all) | 4 | 11 | 6 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 1 / 122 (0.82%) | 6 / 126 (4.76%) |
| occurrences (all) | 7 | 1 | 6 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 8 / 122 (6.56%) | 4 / 126 (3.17%) |
| occurrences (all) | 6 | 13 | 4 |
| Sinusitis | | | |
| subjects affected / exposed | 7 / 119 (5.88%) | 5 / 122 (4.10%) | 8 / 126 (6.35%) |
| occurrences (all) | 7 | 5 | 10 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Refer ClinicalTrials.gov (CL-9709-301-RD,NCT01455194)results of Ciclesonide 160mcg arm baseline period because EUDRACT system does not allow the reporting of data available for the arm, which includes subjects that were not part of target population.

Notes: