



## Clinical trial results:

### Korean Study of "Real-World" Montelukast Use in Mild Asthmatic Children With Concomitant Allergic Rhinitis

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-004748-37  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 24 October 2007 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2           |
| This version publication date  | 02 June 2016 |
| First version publication date | 19 July 2015 |
| Version creation reason        |              |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 0476-367 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00442559 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.  |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.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                       | 24 October 2007 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 24 October 2007 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess real-world effectiveness of montelukast in children (2 to 14 years) with asthma and allergic rhinitis.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. The following additional measures defined for this individual study were in place for the protection of subjects: adjunct daily inhaler (nebulized salbutamol) therapy on an as needed basis; rescue oral, intramuscular, or intravenous corticosteroid therapy for asthma attacks; and addition of inhaled corticosteroids to study treatments for exacerbation from mild to moderate asthma.

Background therapy:

-

Evidence for comparator:

-

|   |                     |
|---|---------------------|
| Actual start date of recruitment                          | 18 January 2005     |
| Long term follow-up planned                               | Yes                 |
| Long term follow-up rationale                             | Scientific research |
| Long term follow-up duration                              | 9 Months            |
| Independent data monitoring committee (IDMC) involvement? | No                  |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 191 |
| Worldwide total number of subjects   | 191                     |
| EEA total number of subjects         | 0                       |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |

|                           |     |
|---------------------------|-----|
| Children (2-11 years)     | 177 |
| Adolescents (12-17 years) | 14  |
| Adults (18-64 years)      | 0   |
| From 65 to 84 years       | 0   |
| 85 years and over         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Conducted at 5 sites in Korea, Feb2005~ Dec2007 in pediatric participants with comorbid mild asthma and allergic rhinitis. Participant's caregiver understands the study procedures and agrees to participate, signing the informed consent form. Additional inclusion and exclusion criteria applied.

### Pre-assignment

Screening details:

Up to 1 week for wash-out - prior to baseline randomization.

### Period 1

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

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Montelukast |

Arm description:

Participants were treated for 12 months after randomization: Participants 2 to 5 years of age took one 4 mg chewable tablet and 6 to 14 years of age took one 5 mg chewable tablet daily in the evening. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | montelukast sodium |
| Investigational medicinal product code |                    |
| Other name                             | Singulair, MK-0476 |
| Pharmaceutical forms                   | Chewable tablet    |
| Routes of administration               | Oral use           |

Dosage and administration details:

Montelukast 4/5 mg tablet (oral chewable), once daily, 12 weeks to up to 12 months

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | Inhaled Corticosteroids (ICS) |
|------------------|-------------------------------|

Arm description:

Participants were treated for 12 months after randomization: Each participant's physician selected the ICS agent, dose, and regimen. If participants had exacerbated from mild to moderate within 12 weeks, ICS was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | inhaled corticosteroid |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Inhalation solution    |
| Routes of administration               | Inhalation use         |

Dosage and administration details:

Inhaled corticosteroid solution, 1-4 puffs daily, 12 weeks to up to 12 months

| <b>Number of subjects in period 1</b> | Montelukast | Inhaled<br>Corticosteroids (ICS) |
|---------------------------------------|-------------|----------------------------------|
| Started                               | 100         | 91                               |
| 12 weeks after randomization          | 68          | 60                               |
| Completed                             | 66          | 56                               |
| Not completed                         | 34          | 35                               |
| Consent withdrawn by subject          | 1           | -                                |
| Lost to follow-up                     | 32          | 34                               |
| Protocol deviation                    | 1           | 1                                |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Montelukast |
|-----------------------|-------------|

Reporting group description:

Participants were treated for 12 months after randomization: Participants 2 to 5 years of age took one 4 mg chewable tablet and 6 to 14 years of age took one 5 mg chewable tablet daily in the evening. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Inhaled Corticosteroids (ICS) |
|-----------------------|-------------------------------|

Reporting group description:

Participants were treated for 12 months after randomization: Each participant's physician selected the ICS agent, dose, and regimen. If participants had exacerbated from mild to moderate within 12 weeks, ICS was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

| Reporting group values | Montelukast | Inhaled Corticosteroids (ICS) | Total |
|------------------------|-------------|-------------------------------|-------|
| Number of subjects     | 100         | 91                            | 191   |
| Age categorical        |             |                               |       |
| Units: Subjects        |             |                               |       |

|   |     |       |     |
|---|-----|-------|-----|
| Age Continuous  |     |       |     |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.                           |     |       |     |
| Units: years  |     |       |     |
| arithmetic mean   | 5.4 | 6.1   |     |
| standard deviation  | ± 3 | ± 2.6 | -   |
| Gender, Male/Female   |     |       |     |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.                           |     |       |     |
| Units: participants   |     |       |     |
| Female  | 5   | 9     | 14  |
| Male  | 19  | 20    | 39  |
| Not reported  | 76  | 62    | 138 |
| Allergic rhinitis   |     |       |     |
| Based on GINA guidelines. The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included. |     |       |     |
| Units: Subjects   |     |       |     |
| Mild-intermittent   | 14  | 17    | 31  |
| Mild-persistent   | 10  | 12    | 22  |
| Not reported  | 76  | 62    | 138 |
| Type of allergic rhinitis   |     |       |     |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.                           |     |       |     |
| Units: Subjects   |     |       |     |
| Seasonal  | 13  | 15    | 28  |
| Perennial   | 11  | 14    | 25  |
| Not reported  | 76  | 62    | 138 |

|   |        |        |   |
|---|--------|--------|---|
| Daily allergic rhinitis symptom score   |        |        |   |
| The secondary efficacy parameter was a mean change from baseline to treatment for daily allergic rhinitis score. Therefore 139 participants who didn't have a daily allergic rhinitis symptom score from the participant diary were not included. |        |        |   |
| Units: Units on scale   |        |        |   |
| arithmetic mean   | 0.45   | 0.31   |   |
| standard deviation  | ± 0.35 | ± 0.34 | - |
| Daytime asthma symptom score  |        |        |   |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.             |        |        |   |
| Units: Units on scale   |        |        |   |
| arithmetic mean   | 0.32   | 0.29   |   |
| standard deviation  | ± 0.42 | ± 0.4  | - |
| Duration of allergic rhinitis   |        |        |   |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.             |        |        |   |
| Units: Years  |        |        |   |
| arithmetic mean   | 0.4    | 0.8    |   |
| standard deviation  | ± 0.6  | ± 1    | - |
| Duration of asthma  |        |        |   |
| The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.             |        |        |   |
| Units: Years  |        |        |   |
| arithmetic mean   | 0.6    | 1.1    |   |
| standard deviation  | ± 0.7  | ± 1.2  | - |

## End points

### End points reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Montelukast |
|-----------------------|-------------|

Reporting group description:

Participants were treated for 12 months after randomization: Participants 2 to 5 years of age took one 4 mg chewable tablet and 6 to 14 years of age took one 5 mg chewable tablet daily in the evening. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Inhaled Corticosteroids (ICS) |
|-----------------------|-------------------------------|

Reporting group description:

Participants were treated for 12 months after randomization: Each participant's physician selected the ICS agent, dose, and regimen. If participants had exacerbated from mild to moderate within 12 weeks, ICS was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daytime Asthma Symptom Score at Baseline - Montelukast |
|----------------------------|--|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daytime Asthma Symptom Score at 12 Weeks - Montelukast |
|----------------------------|--|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daytime Asthma Symptom Score at Baseline - ICS |
|----------------------------|--|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daytime Asthma Symptom Score at 12 Weeks - ICS |
|----------------------------|--|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daily Allergic Rhinitis Symptom Score at Baseline- Montelukast |
|----------------------------|--|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Daily Allergic Rhinitis Symptom Score at 12 Weeks-<br>Montelukast |
|----------------------------|---|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were



excluded in the efficacy evaluation at 12 weeks.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Daily Allergic Rhinitis Symptom Score at Baseline - ICS |
| Subject analysis set type  | Modified intention-to-treat                             |

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Daily Allergic Rhinitis Symptom Score 12 Weeks - ICS |
| Subject analysis set type  | Modified intention-to-treat                          |

Subject analysis set description:

Participants received study drug and had efficacy measurements both at baseline and during the treatment period. If participants had exacerbated from mild to moderate within 12 weeks, inhaled corticosteroids (ICS) was added to Montelukast and ICS, respectively and those participants were excluded in the efficacy evaluation at 12 weeks.

### Primary: Change from Baseline for Daytime Asthma Symptom Score

|                 |   |
|-----------------|---|
| End point title | Change from Baseline for Daytime Asthma Symptom Score |
|-----------------|---|

End point description:

The score is an ordinal scale from 0 (no symptoms) to 5 (most symptoms). The change was calculated as the score at 12 weeks minus the score at baseline (Statistical Analyses: Change from BL to Week 12 - Montelukast; Change from BL to Week 12 - ICS). Thus, a negative value for change from baseline indicates a favorable outcome. The primary efficacy parameter was a mean change from baseline to treatment for daytime asthma symptom score. Therefore 138 participants who didn't have a daytime asthma symptom score from the participant diary were not included.

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

End point timeframe:

Baseline and Week 12

| End point values                     | Daytime Asthma Symptom Score at Baseline - Montelukast | Daytime Asthma Symptom Score at 12 Weeks - Montelukast | Daytime Asthma Symptom Score at Baseline - ICS | Daytime Asthma Symptom Score at 12 Weeks - ICS |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Subject analysis set                                   | Subject analysis set                                   | Subject analysis set                           | Subject analysis set                           |
| Number of subjects analysed          | 24   | 24   | 29   | 29   |
| Units: Units on a scale              |  |  |  |  |
| arithmetic mean (standard deviation) | 0.32 (± 0.42)  | 0.16 (± 0.35)  | 0.29 (± 0.4)                                   | 0.13 (± 0.27)                                  |

### Statistical analyses

|                            |   |
|----------------------------|---|
| Statistical analysis title | Change from BL to Week 12 - Montelukast |
|----------------------------|---|

Statistical analysis description:

The difference in mean change from baseline to 12 weeks in daytime asthma symptom score was tested by paired t-test (H0: difference =0) for the Montelukast treatment group.

|                   |  |
|-------------------|--|
| Comparison groups | Daytime Asthma Symptom Score at Baseline - Montelukast v<br>Daytime Asthma Symptom Score at 12 Weeks - Montelukast |
|-------------------|--|

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 48                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other <sup>[1]</sup>           |
| P-value                                 | = 0.015                        |
| Method                                  | t-test, 2-sided                |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -0.16                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.29                          |
| upper limit                             | -0.03                          |

Notes:

[1] - Subjects in this analysis: N=24 subjects for the within arm (single arm) comparison between BL and Week 12 scores.

|                                   |                                 |
|-----------------------------------|---------------------------------|
| <b>Statistical analysis title</b> | Change from BL to Week 12 - ICS |
|-----------------------------------|---------------------------------|

Statistical analysis description:

The difference in mean change from baseline to 12 weeks in daytime asthma symptom score was tested by paired t-test (H0: difference =0) for the ICS treatment group.

|   |   |
|---|---|
| Comparison groups                       | Daytime Asthma Symptom Score at Baseline - ICS v Daytime Asthma Symptom Score at 12 Weeks - ICS |
| Number of subjects included in analysis | 58  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[2]</sup>  |
| P-value                                 | = 0.027   |
| Method                                  | t-test, 2-sided   |
| Parameter estimate                      | Mean difference (final values)  |
| Point estimate                          | -0.16   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.3  |
| upper limit                             | -0.02   |

Notes:

[2] - Subjects in this analysis: N=29 subjects for the within arm (single arm) comparison between BL and Week 12 scores.

## **Secondary: Change from Baseline for Daily Allergic Rhinitis Symptom Score**

|                 |  |
|-----------------|--|
| End point title | Change from Baseline for Daily Allergic Rhinitis Symptom Score |
|-----------------|--|

End point description:

The score is an ordinal scale from 0 (no symptoms) to 3 (most symptoms). The change was calculated as the score at 12 weeks minus the score at baseline (Statistical Analyses: Change from BL to Week 12 - Montelukast; Change from BL to Week 12 - ICS). Thus, a negative value for change from baseline indicates a favorable outcome. The secondary efficacy parameter was a mean change from baseline to treatment for daily allergic rhinitis symptom score. Therefore 139 participants who didn't have a daily allergic rhinitis symptom score from the participant diary were not included.

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

End point timeframe:

Baseline and Week 12

| <b>End point values</b>              | Daily Allergic Rhinitis Symptom Score at Baseline- Montelukast | Daily Allergic Rhinitis Symptom Score at 12 Weeks- Montelukast | Daily Allergic Rhinitis Symptom Score at Baseline - ICS | Daily Allergic Rhinitis Symptom Score 12 Weeks - ICS |
|--------------------------------------|--|--|---|--|
| Subject group type                   | Subject analysis set   | Subject analysis set   | Subject analysis set                                    | Subject analysis set                                 |
| Number of subjects analysed          | 24   | 24   | 28  | 28   |
| Units: Units on a scale              |  |  |   |  |
| arithmetic mean (standard deviation) | 0.45 (± 0.35)  | 0.23 (± 0.26)  | 0.31 (± 0.34)   | 0.19 (± 0.26)  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Change from BL to Week 12 - Montelukast   |
|--|---|
| Statistical analysis description:<br>The difference in mean change from baseline to 12 weeks in daily allergic rhinitis symptom score was tested by paired t-test (H0: difference =0) for the Montelukast treatment group. |   |
| Comparison groups  | Daily Allergic Rhinitis Symptom Score at Baseline- Montelukast v Daily Allergic Rhinitis Symptom Score at 12 Weeks- Montelukast |
| Number of subjects included in analysis  | 48  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other <sup>[3]</sup>  |
| P-value  | = 0.006   |
| Method   | t-test, 2-sided   |
| Parameter estimate   | Mean difference (final values)  |
| Point estimate   | -0.21   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | -0.36   |
| upper limit  | -0.07   |

Notes:

[3] - Subjects in this analysis: N=24 subjects for the within arm (single arm) comparison between BL and Week 12 scores.

| <b>Statistical analysis title</b>  | Change from BL to Week 12 - ICS  |
|--|--|
| Statistical analysis description:<br>The difference in mean change from baseline to 12 weeks in daily allergic rhinitis symptom score was tested by paired t-test (H0: difference =0) for the ICS treatment group. |  |
| Comparison groups  | Daily Allergic Rhinitis Symptom Score at Baseline - ICS v Daily Allergic Rhinitis Symptom Score 12 Weeks - ICS |
| Number of subjects included in analysis  | 56   |
| Analysis specification   | Pre-specified  |
| Analysis type  | other <sup>[4]</sup>   |
| P-value  | = 0.032  |
| Method   | t-test, 2-sided  |
| Parameter estimate   | Mean difference (final values)   |
| Point estimate   | -0.12  |

| Confidence interval |         |
|---------------------|---------|
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.24   |
| upper limit         | -0.01   |

Notes:

[4] - Subjects in this analysis: N=28 subjects for the within arm (single arm) comparison between BL and Week 12 scores.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 months

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Montelukast |
|-----------------------|-------------|

Reporting group description:

Participants were treated for 12 months after randomization: Participants 2 to 5 years of age took one 4 mg chewable tablet and 6 to 14 years of age took one 5 mg chewable tablet daily in the evening.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Inhaled Corticosteroids (ICS) |
|-----------------------|-------------------------------|

Reporting group description:

Participants were treated for 12 months after randomization: Each participant's physician selected the ICS agent, dose, and regimen.

| Serious adverse events                               | Montelukast     | Inhaled Corticosteroids (ICS) |  |
|--|-----------------|-------------------------------|--|
| Total subjects affected by serious adverse events    |                 |                               |  |
| subjects affected / exposed                          | 4 / 100 (4.00%) | 3 / 91 (3.30%)                |  |
| number of deaths (all causes)                        | 0               | 0                             |  |
| number of deaths resulting from adverse events       |                 |                               |  |
| Nervous system disorders                             |                 |                               |  |
| HEADACHE   |                 |                               |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 91 (1.10%)                |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1                         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                         |  |
| General disorders and administration site conditions |                 |                               |  |
| PYREXIA  |                 |                               |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 91 (1.10%)                |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1                         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                         |  |
| Gastrointestinal disorders                           |                 |                               |  |
| VOMITING   |                 |                               |  |
| subjects affected / exposed                          | 0 / 100 (0.00%) | 1 / 91 (1.10%)                |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1                         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0                         |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| ASTHMA  |                 |                |  |
| subjects affected / exposed                     | 3 / 100 (3.00%) | 2 / 91 (2.20%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| DYSпноEA  |                 |                |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 0 / 91 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| CHRONIC SINUSITIS                               |                 |                |  |
| subjects affected / exposed                     | 0 / 100 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| PNEUMONIA                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Montelukast       | Inhaled Corticosteroids (ICS) |  |
|---|-------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events |                   |                               |  |
| subjects affected / exposed                           | 83 / 100 (83.00%) | 70 / 91 (76.92%)              |  |
| Nervous system disorders                              |                   |                               |  |
| HEADACHE  |                   |                               |  |
| subjects affected / exposed                           | 9 / 100 (9.00%)   | 10 / 91 (10.99%)              |  |
| occurrences (all)                                     | 9                 | 11                            |  |
| General disorders and administration site conditions  |                   |                               |  |
| PYREXIA   |                   |                               |  |
| subjects affected / exposed                           | 31 / 100 (31.00%) | 24 / 91 (26.37%)              |  |
| occurrences (all)                                     | 41                | 34                            |  |
| Gastrointestinal disorders                            |                   |                               |  |
| VOMITING  |                   |                               |  |

|  |                      |                     |  |
|--|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 6 / 100 (6.00%)<br>6 | 7 / 91 (7.69%)<br>7 |  |
| Respiratory, thoracic and mediastinal disorders  |                      |                     |  |
| COUGH  |                      |                     |  |
| subjects affected / exposed                      | 56 / 100 (56.00%)    | 47 / 91 (51.65%)    |  |
| occurrences (all)                                | 88                   | 92                  |  |
| DYSпноEA   |                      |                     |  |
| subjects affected / exposed                      | 7 / 100 (7.00%)      | 5 / 91 (5.49%)      |  |
| occurrences (all)                                | 10                   | 6                   |  |
| NASAL DISCOMFORT                                 |                      |                     |  |
| subjects affected / exposed                      | 15 / 100 (15.00%)    | 8 / 91 (8.79%)      |  |
| occurrences (all)                                | 21                   | 9                   |  |
| OROPHARYNGEAL PAIN                               |                      |                     |  |
| subjects affected / exposed                      | 7 / 100 (7.00%)      | 8 / 91 (8.79%)      |  |
| occurrences (all)                                | 8                    | 10                  |  |
| PRODUCTIVE COUGH                                 |                      |                     |  |
| subjects affected / exposed                      | 12 / 100 (12.00%)    | 12 / 91 (13.19%)    |  |
| occurrences (all)                                | 12                   | 17                  |  |
| RHINORRHOEA                                      |                      |                     |  |
| subjects affected / exposed                      | 27 / 100 (27.00%)    | 21 / 91 (23.08%)    |  |
| occurrences (all)                                | 36                   | 30                  |  |
| UPPER AIRWAY OBSTRUCTION                         |                      |                     |  |
| subjects affected / exposed                      | 30 / 100 (30.00%)    | 30 / 91 (32.97%)    |  |
| occurrences (all)                                | 42                   | 43                  |  |
| SNEEZING   |                      |                     |  |
| subjects affected / exposed                      | 21 / 100 (21.00%)    | 18 / 91 (19.78%)    |  |
| occurrences (all)                                | 29                   | 26                  |  |
| WHEEZING   |                      |                     |  |
| subjects affected / exposed                      | 9 / 100 (9.00%)      | 13 / 91 (14.29%)    |  |
| occurrences (all)                                | 10                   | 15                  |  |
| Infections and infestations                      |                      |                     |  |
| NASOPHARYNGITIS                                  |                      |                     |  |
| subjects affected / exposed                      | 6 / 100 (6.00%)      | 2 / 91 (2.20%)      |  |
| occurrences (all)                                | 6                    | 2                   |  |
| UPPER RESPIRATORY TRACT INFECTION                |                      |                     |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 9 / 100 (9.00%) | 7 / 91 (7.69%) |  |
| occurrences (all)           | 9               | 10             |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### 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.

|  |
|--|
| This was an open-label study. Only 53 patients had diary information with daytime asthma symptom score - thus, 138 cases were dropped from analysis due to lack of daytime asthma symptom score. |
|--|

Notes: