



Clinical trial results:

Randomized, Placebo-Controlled Clinical Trial to Study the Efficacy and Safety of Inhaled Corticosteroid Plus Montelukast Compared with Inhaled Corticosteroid Therapy Alone in Patients with Chronic Asthma Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2007-006097-28 |
| Trial protocol | GB |
| Global end of trial date | 16 February 2009 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 13 April 2016 |
| First version publication date | 09 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 0476-386 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00666679 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | MK-0476-386: Merck Registration |

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., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., 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 | 16 February 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 February 2009 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 February 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate that treatment with montelukast and mometasone (an inhaled corticosteroid), compared with mometasone alone, results in improvement in Forced Expiratory Volume in 1 Second (FEV1) in participants aged 15 to 85 years with chronic asthma; 2) To determine the safety and tolerability of montelukast and mometasone, compared with mometasone alone, in participants aged 15 to 85 years with chronic asthma.

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 measure defined for this individual study was in place for the protection of trial subjects:

Subjects were provided with open-label inhaled corticosteroid (mometasone furoate) for asthma control throughout the study.

Background therapy:

Subjects were provided with open-label inhaled corticosteroid (mometasone furoate) for asthma control throughout the study.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 15 April 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | Colombia: 9 |
| Country: Number of subjects enrolled | Israel: 26 |
| Country: Number of subjects enrolled | Peru: 55 |
| Country: Number of subjects enrolled | United States: 33 |
| Worldwide total number of subjects | 134 |
| 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) | 0 |
| Adolescents (12-17 years) | 10 |
| Adults (18-64 years) | 115 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were screened who were nonsmoking males and females aged 15 to 85 years, had chronic asthma, had an FEV1 50-80% of predicted while withholding short-acting β -agonist (SABA) and demonstrated reversibility of airway obstruction >12% following SABA administration.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Montelukast+Mometasone then Placebo+Mometasone |

Arm description:

Participants received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | montelukast |
| Investigational medicinal product code | |
| Other name | MK-0476 |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

Montelukast 1 mg via dry powder inhaler by inhalation once daily at bedtime

| | |
|--|----------------------|
| Investigational medicinal product name | mometasone |
| Investigational medicinal product code | |
| Other name | ASMANEX™ TWISTHALER™ |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Mometasone 220 mcg via dry powder inhaler by inhalation once daily at bedtime

| | |
|------------------|--|
| Arm title | Placebo+Mometasone then Montelukast+Mometasone |
|------------------|--|

Arm description:

Participants received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|----------------------|
| Investigational medicinal product name | mometasone |
| Investigational medicinal product code | |
| Other name | ASMANEX™ TWISTHALER™ |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Mometasone 220 mcg via dry powder inhaler by inhalation once daily at bedtime

| | |
|--|---------------------------------|
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo via dry powder inhaler by inhalation once daily at bedtime

| Number of subjects in period 1 | Montelukast+Mometasone then Placebo+Mometasone | Placebo+Mometasone then Montelukast+Mometasone |
|--------------------------------|--|--|
| Started | 66 | 68 |
| Treated | 65 | 67 |
| Completed | 62 | 65 |
| Not completed | 4 | 3 |
| Consent withdrawn by subject | 1 | - |
| Lost to follow-up | 1 | 1 |
| Protocol deviation | 1 | 1 |
| Not treated | 1 | 1 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Treatment Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Montelukast+Mometasone then Placebo+Mometasone |

Arm description:

Participants received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|----------------------|
| Investigational medicinal product name | mometasone |
| Investigational medicinal product code | |
| Other name | ASMANEX™ TWISTHALER™ |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Mometasone 220 mcg via dry powder inhaler by inhalation once daily at bedtime

| | |
|--|---------------------------------|
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

Placebo via dry powder inhaler by inhalation once daily at bedtime

| | |
|------------------|--|
| Arm title | Placebo+Mometasone then Montelukast+Mometasone |
|------------------|--|

Arm description:

Participants received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | montelukast |
| Investigational medicinal product code | |
| Other name | MK-0476 |
| Pharmaceutical forms | Inhalation powder, hard capsule |
| Routes of administration | Inhalation use |

Dosage and administration details:

Montelukast 1 mg via dry powder inhaler by inhalation once daily at bedtime

| | |
|--|----------------------|
| Investigational medicinal product name | mometasone |
| Investigational medicinal product code | |
| Other name | ASMANEX™ TWISTHALER™ |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

Mometasone 220 mcg via dry powder inhaler by inhalation once daily at bedtime

| Number of subjects in period 2 | Montelukast+Mometasone then Placebo+Mometasone | Placebo+Mometasone then Montelukast+Mometasone |
|---------------------------------------|--|--|
| Started | 62 | 65 |
| Completed | 61 | 64 |
| Not completed | 1 | 1 |
| Adverse event, serious fatal | - | 1 |
| Adverse event, non-fatal | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Montelukast+Mometasone then Placebo+Mometasone |
| Reporting group description: | |
| Participants received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation. | |
| Reporting group title | Placebo+Mometasone then Montelukast+Mometasone |
| Reporting group description: | |
| Participants received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation. | |

| Reporting group values | Montelukast+Mometasone then Placebo+Mometasone | Placebo+Mometasone then Montelukast+Mometasone | Total |
|--|--|--|-------|
| Number of subjects | 66 | 68 | 134 |
| Age categorical Units: Subjects | | | |
| Adolescents (12-17 years) | 6 | 4 | 10 |
| Adults (18-64 years) | 57 | 58 | 115 |
| From 65-84 years | 3 | 6 | 9 |
| Gender categorical Units: Subjects | | | |
| Female | 37 | 32 | 69 |
| Male | 29 | 36 | 65 |
| FEV1 | | | |
| FEV1 is the amount of air (in liters) forcibly exhaled during the first second of exhalation. Baseline FEV1 was defined as the last pre β -agonist value obtained prior to randomization. | | | |
| Units: liters | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | - |
| Daytime Asthma Symptoms Score | | | |
| In the evening just before going to bed, participants scored their asthma symptoms over the period since arising by answering the following 4 questions in a daily diary: 1) How often did you experience asthma symptoms today?; 2) How much did your asthma symptoms bother you?; 3) How much activity could you do today?; and 4) How often did your asthma affect your activities today? Daytime asthma symptoms were assessed on a 7-point scale (0=best to 6=worst). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | - |
| Nighttime Asthma Symptoms Score | | | |
| In the morning, upon arising, and before taking any medications, participants answered the following question in a daily diary concerning the overnight period: Did you wake up with asthma symptoms? Nighttime asthma symptoms were assessed on a 4-point scale (0=No to 3=Awake all night). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | - |

Subject analysis sets

| | |
|--|--|
| Subject analysis set title | Montelukast+Mometasone Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who received ≥ 1 dose montelukast plus mometasone and had Baseline and post-treatment data. | |
| Subject analysis set title | Placebo+Mometasone Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who received ≥ 1 dose placebo plus mometasone and had Baseline and post-treatment data. | |
| Subject analysis set title | Montelukast+Mometasone Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants who received ≥ 1 dose of montelukast plus mometasone | |
| Subject analysis set title | Placebo+Mometasone Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants who received ≥ 1 dose of placebo plus mometasone | |

| Reporting group values | Montelukast+Mometasone Full Analysis Set | Placebo+Mometasone Full Analysis Set | Montelukast+Mometasone Safety Set |
|--|--|--------------------------------------|-----------------------------------|
| Number of subjects | 127 | 127 | 130 |
| Age categorical Units: Subjects | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| Gender categorical Units: Subjects | | | |
| Female | | | |
| Male | | | |
| FEV1 | | | |
| FEV1 is the amount of air (in liters) forcibly exhaled during the first second of exhalation. Baseline FEV1 was defined as the last pre β -agonist value obtained prior to randomization. | | | |
| Units: liters | | | |
| arithmetic mean | 2.18 | 2.19 | |
| standard deviation | ± 0.6 | ± 0.61 | \pm |
| Daytime Asthma Symptoms Score | | | |
| In the evening just before going to bed, participants scored their asthma symptoms over the period since arising by answering the following 4 questions in a daily diary: 1) How often did you experience asthma symptoms today?; 2) How much did your asthma symptoms bother you?; 3) How much activity could you do today?; and 4) How often did your asthma affect your activities today? Daytime asthma symptoms were assessed on a 7-point scale (0=best to 6=worst). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | 2.1 | 2.12 | |
| standard deviation | ± 0.85 | ± 0.85 | \pm |
| Nighttime Asthma Symptoms Score | | | |
| In the morning, upon arising, and before taking any medications, participants answered the following question in a daily diary concerning the overnight period: Did you wake up with asthma symptoms? Nighttime asthma symptoms were assessed on a 4-point scale (0=No to 3=Awake all night). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | 0.7 | 0.71 | |

| | | | |
|--------------------|--------|--------|---|
| standard deviation | ± 0.46 | ± 0.46 | ± |
|--------------------|--------|--------|---|

| Reporting group values | Placebo+Mometason e Safety Set | | |
|--|-----------------------------------|--|--|
| Number of subjects | 129 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| FEV1 | | | |
| FEV1 is the amount of air (in liters) forcibly exhaled during the first second of exhalation. Baseline FEV1 was defined as the last pre β -agonist value obtained prior to randomization. | | | |
| Units: liters | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Daytime Asthma Symptoms Score | | | |
| In the evening just before going to bed, participants scored their asthma symptoms over the period since arising by answering the following 4 questions in a daily diary: 1) How often did you experience asthma symptoms today?; 2) How much did your asthma symptoms bother you?; 3) How much activity could you do today?; and 4) How often did your asthma affect your activities today? Daytime asthma symptoms were assessed on a 7-point scale (0=best to 6=worst). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Nighttime Asthma Symptoms Score | | | |
| In the morning, upon arising, and before taking any medications, participants answered the following question in a daily diary concerning the overnight period: Did you wake up with asthma symptoms? Nighttime asthma symptoms were assessed on a 4-point scale (0=No to 3=Awake all night). | | | |
| Units: Score on a Scale | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Montelukast+Mometasone then Placebo+Mometasone |
|-----------------------|--|

Reporting group description:

Participants received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|-----------------------|--|
| Reporting group title | Placebo+Mometasone then Montelukast+Mometasone |
|-----------------------|--|

Reporting group description:

Participants received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|-----------------------|--|
| Reporting group title | Montelukast+Mometasone then Placebo+Mometasone |
|-----------------------|--|

Reporting group description:

Participants received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|-----------------------|--|
| Reporting group title | Placebo+Mometasone then Montelukast+Mometasone |
|-----------------------|--|

Reporting group description:

Participants received placebo plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 1 and received montelukast 1 mg plus open-label mometasone 220 mcg by inhalation once daily for 2 weeks in Treatment Period 2. Treatment Periods 1 and 2 were separated by a 1-week wash-out period during which all participants received open-label mometasone plus blinded placebo by inhalation.

| | |
|----------------------------|--|
| Subject analysis set title | Montelukast+Mometasone Full Analysis Set |
|----------------------------|--|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants who received ≥ 1 dose montelukast plus mometasone and had Baseline and post-treatment data.

| | |
|----------------------------|--------------------------------------|
| Subject analysis set title | Placebo+Mometasone Full Analysis Set |
|----------------------------|--------------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants who received ≥ 1 dose placebo plus mometasone and had Baseline and post-treatment data.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Montelukast+Mometasone Safety Set |
|----------------------------|-----------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Participants who received ≥ 1 dose of montelukast plus mometasone

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Placebo+Mometasone Safety Set |
|----------------------------|-------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Participants who received ≥ 1 dose of placebo plus mometasone

Primary: Average Change from Baseline in FEV1 Over 2 Weeks

| | |
|-----------------|---|
| End point title | Average Change from Baseline in FEV1 Over 2 Weeks |
|-----------------|---|

End point description:

FEV1 is the amount of air (in liters) forcibly exhaled during the first second of exhalation. FEV1 was assessed 1 and 2 weeks after start of treatment. Changes from Baseline in FEV1 at Weeks 1 and 2 of treatment were averaged.

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

End point timeframe:
Over 2-week treatment period

| End point values | Montelukast+Mometasone Full Analysis Set | Placebo+Mometasone Full Analysis Set | | |
|--|--|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 127 ^[1] | 127 ^[2] | | |
| Units: liters | | | | |
| least squares mean (confidence interval 95%) | 0.22 (0.15 to 0.3) | 0.17 (0.11 to 0.23) | | |

Notes:

[1] - Participants who received ≥ 1 dose montelukast+mometasone and had Baseline and post-treatment data.

[2] - Participants who received ≥ 1 dose placebo+mometasone and had Baseline and post-treatment data.

Statistical analyses

| Statistical analysis title | Difference in FEV1 After Treatment |
|----------------------------|------------------------------------|
|----------------------------|------------------------------------|

Statistical analysis description:

The difference in least squares (LS) means of Montelukast+Mometasone compared to Placebo+Mometasone for FEV1 was analyzed using a longitudinal data analysis (LDA) model that included terms for treatment, time (Weeks 1 and 2), treatment-by-time interaction, period and Baseline FEV1 as a covariate.

| | |
|---|---|
| Comparison groups | Placebo+Mometasone Full Analysis Set v Montelukast+Mometasone Full Analysis Set |
| Number of subjects included in analysis | 254 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.033 |
| Method | LDA |
| Parameter estimate | Difference in LS Means |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.09 |

Notes:

[3] - Based on repeated measures analysis model using repeated measurements at 2 study times (Weeks 1 and 2) with fixed effects for treatment, time, treatment-by-time interaction, period and Baseline FEV1.

Secondary: Change from Baseline in Daytime Asthma Symptom Score

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

End point description:

In the evening just before going to bed, participants scored their asthma symptoms over the period since arising by answering the following 4 questions in a daily diary: 1) How often did you experience asthma symptoms today?; 2) How much did your asthma symptoms bother you?; 3) How much activity could you do today?; and 4) How often did your asthma affect your activities today? Daytime asthma symptoms were assessed on a 7-point scale (0=best to 6=worst) after 1 and 2 weeks of treatment. Changes from baseline in daytime asthma symptom score by day are averaged over the diary days belonging to a specific time period (so Week 1 or 2) and the average over these 2 periods was then obtained in the model. The average change from Baseline in daytime asthma symptom score was

calculated.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 2 Weeks | |

| End point values | Montelukast+Mometasone Full Analysis Set | Placebo+Mometasone Full Analysis Set | | |
|--|--|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 128 ^[4] | 129 ^[5] | | |
| Units: Score on a Scale | | | | |
| least squares mean (confidence interval 95%) | -0.39 (-0.49 to -0.29) | -0.24 (-0.35 to -0.12) | | |

Notes:

[4] - Participants who received ≥ 1 dose montelukast+mometasone and had Baseline and post-treatment data.

[5] - Participants who received ≥ 1 dose placebo+mometasone and had Baseline and post-treatment data.

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Difference in Daytime Asthma Symptom Scores |
|----------------------------|---|

Statistical analysis description:

The difference in LS means of Montelukast+Mometasone compared to Placebo+Mometasone for daytime asthma symptom score was analyzed using an LDA model that included terms for treatment, time (Weeks 1 and 2), treatment-by-time interaction, period and Baseline daytime asthma symptom score as a covariate.

| | |
|---|---|
| Comparison groups | Montelukast+Mometasone Full Analysis Set v Placebo+Mometasone Full Analysis Set |
| Number of subjects included in analysis | 257 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | = 0.005 |
| Method | LDA |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.26 |
| upper limit | -0.05 |

Notes:

[6] - Based on repeated measures analysis model using repeated measurements at two study times (Weeks 1 and 2) with fixed effects for treatment, time, treatment-by-time interaction, period and Baseline daytime asthma symptom score.

Secondary: Change from Baseline in Nighttime Asthma Symptom Score

| | |
|-----------------|--|
| End point title | Change from Baseline in Nighttime Asthma Symptom Score |
|-----------------|--|

End point description:

In the morning, upon arising, and before taking any medications, participants answered the following question in a daily diary concerning the overnight period: Did you wake up with asthma symptoms? Nighttime asthma symptoms were assessed on a 4-point scale (0=No to 3=Awake all night) at Baseline and after 1 and 2 weeks of treatment. Changes from baseline in nighttime asthma symptom score by day are averaged over the diary days belonging to a specific time period (so Week 1 or 2) and the

average over these 2 periods was then obtained in the model. The average change from Baseline in nighttime asthma symptom score was calculated.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 2 Weeks | |

| End point values | Montelukast+Mometasone Full Analysis Set | Placebo+Mometasone Full Analysis Set | | |
|--|--|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 89 ^[7] | 90 ^[8] | | |
| Units: Score on a Scale | | | | |
| least squares mean (confidence interval 95%) | -0.28 (-0.35 to -0.2) | -0.18 (-0.28 to -0.09) | | |

Notes:

[7] - Participants who received ≥ 1 dose montelukast+mometasone and had Baseline and post-treatment data.

[8] - Participants who received ≥ 1 dose placebo+mometasone and had Baseline and post-treatment data.

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in Nighttime Asthma Symptom Scores |
|-----------------------------------|---|

Statistical analysis description:

The difference in LS means of Montelukast+Mometasone compared to Placebo+Mometasone for nighttime asthma symptom score was analyzed using an LDA model that included terms for treatment, time (Weeks 1 and 2), treatment-by-time interaction, period and Baseline nighttime asthma symptom score as a covariate.

| | |
|---|---|
| Comparison groups | Montelukast+Mometasone Full Analysis Set v Placebo+Mometasone Full Analysis Set |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | = 0.015 |
| Method | LDA |
| Parameter estimate | Difference in LS Means |
| Point estimate | -0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.17 |
| upper limit | -0.02 |

Notes:

[9] - Based on repeated measures analysis model using repeated measurements at two study times (Weeks 1 and 2) with fixed effects for treatment, time, treatment-by-time interaction, period and Baseline nighttime asthma symptom score.

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to 1 week after last dose of study drug in a treatment period (Up to 3 weeks in a treatment period; up to 6 weeks total for the study)

Adverse event reporting additional description:

Includes all participants who received ≥ 1 dose of study drug in ≥ 1 of the 2 study periods. Participants are included in the treatment group corresponding to the study drug they actually received. Adverse events occurring during the washout period between the two treatment periods are counted towards the earlier treatment period.

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

Dictionary used

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

Reporting groups

| | |
|-----------------------|------------------------|
| Reporting group title | Montelukast+Mometasone |
|-----------------------|------------------------|

Reporting group description:

Participants who received ≥ 1 dose of montelukast plus mometasone.

| | |
|-----------------------|--------------------|
| Reporting group title | Placebo+Mometasone |
|-----------------------|--------------------|

Reporting group description:

Participants who received ≥ 1 dose of placebo plus mometasone.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events occurred in $>5\%$ of participants in either treatment group.

| Serious adverse events | Montelukast+Mometasone | Placebo+Mometasone | |
|---|------------------------|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 129 (0.78%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

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

| Non-serious adverse events | Montelukast+Mometasone | Placebo+Mometasone | |
|---|------------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 0 / 129 (0.00%) | |

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

None reported