



Clinical trial results:

A Phase 3, 12-Week, Double-Blind, Randomized, Parallel-Group, Multicenter Study Investigating the Efficacy and Safety of Symbicort pMDI 80/2.25 g, 2 Actuations Twice Daily, and Symbicort pMDI 80/4.5 g, 2 Actuations Twice Daily, Compared with Budesonide pMDI 80 g, 2 Actuations Twice Daily, in Children Ages 6 to <12 Years with Asthma Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-005293-22 |
| Trial protocol | SK |
| Global end of trial date | 14 April 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 27 October 2016 |
| First version publication date | 27 October 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D589GC00003 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | Pepparedsleden 1, Mölndal, Sweden, |
| Public contact | Global Clinical Lead Göran Eckerwall, AstraZeneca, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead Göran Eckerwall, Astrazeneca Research and Development, 0046 +46 31 7761000, information.center@astrazeneca.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? | No |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 24 May 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 April 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 April 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate the efficacy of Symbicort pMDI 80/4.5, 2 inhalations bid and Symbicort pMDI 80/2.25, 2 inhalations bid, compared with budesonide pMDI 80 µg, 2 inhalations bid, in children ages 6 to <12 years with asthma.

Protection of trial subjects:

Before subjects can be enrolled into the study or starting the study procedure, an informed consent and child assent forms following the relevant local regulations of subject protection and data privacy must be signed by the subjects and their legal guardian(s).

The study data was stored in a computer database, maintaining confidentiality in accordance with relevant regulations. All data computer-processed by AstraZeneca or representative will be identified by patient enrollment number, randomization number, and study code. The master informed consent and child assent forms will also explain that for data verification purposes, authorized representatives of AstraZeneca, a regulatory authority, an IRB or Independent Ethics Committee (IEC) may require direct access to parts of the hospital or practice records relevant to the study, including the patient's medical history.

The study protocol, Informed Consent/Child Assent Forms and any other written information and/or materials to be provided to the patients were approved by the Institutional Review Board or Ethic committee in accordance with local country regulations.

Patient safety was monitored by the CRO, Quintiles safety group throughout the study conduct. Any reportable adverse events were submitted to the relevant regulatory authorities including IRBs/ECs according to local requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 14 April 2014 |
| 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 | United States: 226 |
| Country: Number of subjects enrolled | Panama: 25 |
| Country: Number of subjects enrolled | Mexico: 8 |
| Country: Number of subjects enrolled | Slovakia: 20 |
| Worldwide total number of subjects | 279 |
| EEA total number of subjects | 20 |

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) | 279 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

881 patients were screened; 237 patients were screen failures and 644 patients received run in medication. Of the patients who received run-in medication, 365 patients were not randomized and 279 patients were randomized.

Period 1

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

Arms

| | |
|------------------------------|--------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Symbicort pMDI 80/4.5 ug |

Arm description:

Symbicort pMDI 80/4.5 ug x 2 BID

| | |
|--|--------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Budesonide/formoterol pMDI 80/4.5 ug |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

pMDI HFA for oral inhalation with ACM budesonide/formoterol fumarate dihydrate

| | |
|------------------|---------------------------|
| Arm title | Symbicort pMDI 80/2.25 ug |
|------------------|---------------------------|

Arm description:

Symbicort pMDI 80/2.25 ug x 2 BID

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Budesonide/formoterol pMDI 80/2.25 ug |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

pMDI HFA for oral inhalation with ACM budesonide/formoterol fumarate dihydrate 80/2.25 ug

| | |
|------------------|-----------------------|
| Arm title | Budesonide pMDI 80 ug |
|------------------|-----------------------|

Arm description:

Budesonide pMDI 80 ug x 2 BID

| | |
|--|-----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Budesonide pMDI 80 ug |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

| Number of subjects in period 1 | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug |
|---------------------------------------|-----------------------------|------------------------------|--------------------------|
| Started | 92 | 95 | 92 |
| Completed | 85 | 84 | 84 |
| Not completed | 7 | 11 | 8 |
| Consent withdrawn by subject | 4 | 8 | 3 |
| Adverse event, non-fatal | - | - | 2 |
| 7 rand in error 1 patient decision | 2 | 3 | 3 |
| Lost to follow-up | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|---|---------------------------|
| Reporting group title | Symbicort pMDI 80/4.5 ug |
| Reporting group description: Symbicort pMDI 80/4.5 ug x 2 BID | |
| Reporting group title | Symbicort pMDI 80/2.25 ug |
| Reporting group description: Symbicort pMDI 80/2.25 ug x 2 BID | |
| Reporting group title | Budesonide pMDI 80 ug |
| Reporting group description: Budesonide pMDI 80 ug x 2 BID | |

| Reporting group values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug |
|--|--------------------------|---------------------------|-----------------------|
| Number of subjects | 92 | 95 | 92 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 92 | 95 | 92 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 9 | 9 | 9 |
| standard deviation | ± 1.6 | ± 1.6 | ± 1.4 |
| Gender, Male/Female | | | |
| Units: Participants | | | |
| Female | 42 | 34 | 37 |
| Male | 50 | 61 | 55 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 3 | 3 |
| Asian | 0 | 0 | 2 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 0 |
| Black or African American | 24 | 26 | 26 |
| White | 61 | 60 | 53 |
| More than one race | 4 | 4 | 7 |
| Unknown or Not Reported | 0 | 2 | 1 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 38 | 36 | 32 |

| | | | |
|-------------------------|----|----|----|
| Not Hispanic or Latino | 54 | 59 | 60 |
| Unknown or Not Reported | 0 | 0 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| Body weight Units: kg arithmetic mean standard deviation | 38 ± 12.9 | 38 ± 12.9 | 40 ± 13.6 |
| Height Units: cm arithmetic mean standard deviation | 139 ± 11.1 | 138 ± 10.9 | 141 ± 10.5 |
| Duration of asthma Units: years arithmetic mean standard deviation | 5.8 ± 3 | 5.9 ± 3.3 | 6.2 ± 3.1 |
| FEV1 at randomisation Units: Liters arithmetic mean standard deviation | 1.58 ± 0.42 | 1.57 ± 0.33 | 1.62 ± 0.36 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 279 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 279 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Gender, Male/Female Units: Participants | | | |
| Female | 113 | | |
| Male | 166 | | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 8 | | |
| Asian | 2 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |
| Black or African American | 76 | | |
| White | 174 | | |
| More than one race | 15 | | |

| | | | |
|-------------------------|-----|--|--|
| Unknown or Not Reported | 3 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 106 | | |
| Not Hispanic or Latino | 173 | | |
| Unknown or Not Reported | 0 | | |
| Body weight | | | |
| Units: kg | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Duration of asthma | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| FEV1 at randomisation | | | |
| Units: Liters | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|-----------------------------------|---------------------------|
| Reporting group title | Symbicort pMDI 80/4.5 ug |
| Reporting group description: | |
| Symbicort pMDI 80/4.5 ug x 2 BID | |
| Reporting group title | Symbicort pMDI 80/2.25 ug |
| Reporting group description: | |
| Symbicort pMDI 80/2.25 ug x 2 BID | |
| Reporting group title | Budesonide pMDI 80 ug |
| Reporting group description: | |
| Budesonide pMDI 80 ug x 2 BID | |

Primary: Change from baseline to Week 12 in 1h post-dose FEV1

| | |
|--|--|
| End point title | Change from baseline to Week 12 in 1h post-dose FEV1 |
| End point description: | |
| 1h post-dose FEV1 is defined as the 1-hour post-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Primary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 93 | 90 | |
| Units: Liters | | | | |
| least squares mean (confidence interval 95%) | 0.28 (0.22 to 0.34) | 0.24 (0.18 to 0.31) | 0.17 (0.1 to 0.23) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | FEV1 1h post-dose Change from baseline to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 ^[1] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.12 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.03 |
| upper limit | 0.2 |

Notes:

[1] - 2-sided p-value

| | |
|---|--|
| Statistical analysis title | FEV1 1h post-dose Change from baseline to week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.373 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | 0.12 |

Notes:

[2] - 2-sided

| | |
|---|---|
| Statistical analysis title | FEV1 1h post-dose Change from baseline to week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 183 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.063 ^[3] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.08 |
| upper limit | 0.16 |

Notes:

[3] - 2-sided

Secondary: Change from baseline to Week 12 in 1h post-dose PEF

| | |
|---|---|
| End point title | Change from baseline to Week 12 in 1h post-dose PEF |
| End point description: | |
| 1h post-dose PEF is defined as the 1-hour post-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |

End point timeframe:

Week 12

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|---|--------------------------------|---------------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 93 | 90 | |
| Units: Liters per minute | | | | |
| least squares mean (confidence interval 95%) | 57.04 (46.12 to 67.97) | 41.14 (30.26 to 52.01) | 31.57 (20.78 to 42.36) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | PEF 1h post dose Change from baseline to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 ^[4] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 25.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.94 |
| upper limit | 40 |

Notes:

[4] - 2-sided

| | |
|---|---|
| Statistical analysis title | PEF 1h post dose Change from baseline to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 183 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.195 ^[5] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 9.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.92 |
| upper limit | 24.05 |

Notes:

[5] - 2-sided

| | |
|---|--|
| Statistical analysis title | PEF 1h post dose Change from baseline to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.032 ^[6] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 15.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.34 |
| upper limit | 30.47 |

Notes:

[6] - 2-sided

Secondary: Change from baseline to Week 12 in 1h post-dose FEF25-75

| | |
|--|--|
| End point title | Change from baseline to Week 12 in 1h post-dose FEF25-75 |
| End point description: | |
| 1h post-dose FEF25-75 is defined as the 1-hour post-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 93 | 90 | |
| Units: Liters per second | | | | |
| least squares mean (confidence interval 95%) | 0.55 (0.43 to 0.67) | 0.47 (0.35 to 0.59) | 0.23 (0.11 to 0.35) | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | FEF25-75 1h post-dose Change from basel to week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 ^[7] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.15 |
| upper limit | 0.48 |

Notes:

[7] - 2-sided

| | |
|---|--|
| Statistical analysis title | FEF25-75 1h post-dose Change from basel to week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 183 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.07 |
| upper limit | 0.4 |

| | |
|---|--|
| Statistical analysis title | FEF25-75 1h post-dose Change from basel to week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.326 ^[8] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.08 |
| upper limit | 0.25 |

Notes:

[8] - 2-sided

Secondary: Change from baseline to Week 12 in 1h post-dose FVC

| | |
|---|---|
| End point title | Change from baseline to Week 12 in 1h post-dose FVC |
| End point description: | |
| 1h post-dose FVC is defined as the 1-hour post-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 93 | 90 | |
| Units: Liters | | | | |
| least squares mean (confidence interval 95%) | 0.22 (0.15 to 0.3) | 0.16 (0.09 to 0.23) | 0.17 (0.1 to 0.24) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | FVC 1h post dose Change from basel to week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.276 ^[9] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.04 |
| upper limit | 0.15 |

Notes:

[9] - 2-sided

| | |
|---|--|
| Statistical analysis title | FVC 1h post dose Change from basel to week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.165 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.07 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.03 |
| upper limit | 0.16 |

| | |
|---|---|
| Statistical analysis title | FVC 1h post dose Change from basel to week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 183 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.759 ^[10] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.11 |
| upper limit | 0.08 |

Notes:

[10] - 2-sided

Secondary: Change from baseline to Week 12 in pre-dose FEV1

| | |
|--|--|
| End point title | Change from baseline to Week 12 in pre-dose FEV1 |
| End point description: | |
| Pre-dose FEV1 is defined as the pre-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------|---------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 92 | 89 | |
| Units: Liters | | | | |
| least squares mean (confidence interval 95%) | 0.11 (0.04 to 0.17) | 0.1 (0.03 to 0.16) | 0.09 (0.03 to 0.15) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | FEV1 pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.724 ^[11] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.07 |
| upper limit | 0.1 |

Notes:

[11] - 2-sided

| | |
|---|---|
| Statistical analysis title | FEV1 pre-dose Change from basel to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.909 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.08 |
| upper limit | 0.09 |

| | |
|---|--|
| Statistical analysis title | FEV1 pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.811 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.07 |
| upper limit | 0.09 |

Secondary: Change from baseline to Week 12 in pre-dose PEF

| | |
|-----------------|---|
| End point title | Change from baseline to Week 12 in pre-dose PEF |
|-----------------|---|

End point description:

Pre-dose PEF is defined as the pre-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued).

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

End point timeframe:

Week 12

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 92 | 89 | |
| Units: Liters per minute | | | | |
| least squares mean (confidence interval 95%) | 27.73 (16.37 to 39.08) | 15.86 (4.39 to 27.33) | 16.01 (4.5 to 27.52) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | PEF pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.134 ^[12] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 11.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.63 |
| upper limit | 27.06 |

Notes:

[12] - 2-sided

| | |
|-----------------------------------|---|
| Statistical analysis title | PEF pre-dose Change from basel to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.985 ^[13] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.28 |
| upper limit | 15.28 |

Notes:

[13] - 2-sided

| | |
|---|--|
| Statistical analysis title | FEV1 pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.128 ^[14] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 11.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.43 |
| upper limit | 27.16 |

Notes:

[14] - 2-sided

Secondary: Change from baseline to Week 12 in pre-dose FEF25-75

| | |
|--|--|
| End point title | Change from baseline to Week 12 in pre-dose FEF25-75 |
| End point description: | |
| Pre-dose FEF25-75 is defined as the pre-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 92 | 89 | |
| Units: Liters per minute | | | | |
| least squares mean (confidence interval 95%) | 0.12 (0.01 to 0.24) | 0.13 (0.01 to 0.25) | 0.09 (-0.03 to 0.21) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | FEF25-75 pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.684 ^[15] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.19 |

Notes:

[15] - 2-sided

| | |
|---|---|
| Statistical analysis title | FEF25-75 pre-dose Change from basel to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.621 ^[16] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.2 |

Notes:

[16] - 2-sided

| | |
|-----------------------------------|--|
| Statistical analysis title | FEF25-75 pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.929 ^[17] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.16 |
| upper limit | 0.15 |

Notes:

[17] - 2-sided

Secondary: Change from baseline to Week 12 in pre-dose FVC

| | |
|---|---|
| End point title | Change from baseline to Week 12 in pre-dose FVC |
| End point description: | |
| Pre-dose FVC is defined as the pre-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 92 | 89 | |
| Units: Liters | | | | |
| least squares mean (confidence interval 95%) | 0.11 (0.03 to 0.18) | 0.11 (0.04 to 0.19) | 0.13 (0.05 to 0.2) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | FVC pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.664 ^[18] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.02 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.08 |

Notes:

[18] - 2-sided

| | |
|---|---|
| Statistical analysis title | FVC pre-dose Change from basel to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.747 ^[19] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.08 |

Notes:

[19] - 2-sided

| | |
|---|--|
| Statistical analysis title | FVC pre-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.913 ^[20] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.11 |
| upper limit | 0.09 |

Notes:

[20] - 2-sided

Secondary: Change from baseline to Week 12 in 15 min post-dose FEV1

| | |
|--|--|
| End point title | Change from baseline to Week 12 in 15 min post-dose FEV1 |
| End point description: | |
| 15 min Post-dose FEV1 is defined as the 15 min post-dose measurement taken at Week 12 minus the pre dose measurement taken at randomization for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |

End point timeframe:

Week 12

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|---|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 79 | 78 | 80 | |
| Units: Liters | | | | |
| least squares mean (confidence interval 95%) | 0.25 (0.18 to 0.31) | 0.19 (0.12 to 0.25) | 0.15 (0.08 to 0.21) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | FEV1 15m post-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 159 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.015 ^[21] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.02 |
| upper limit | 0.18 |

Notes:

[21] - 2-sided

| | |
|---|---|
| Statistical analysis title | FEV1 15m post-dose Change from basel to Week 12 |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 158 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.342 ^[22] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.04 |
| upper limit | 0.12 |

Notes:

[22] - 2-sided

| | |
|---|--|
| Statistical analysis title | FEV1 15m post-dose Change from basel to Week 12 |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 157 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.138 ^[23] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.02 |
| upper limit | 0.15 |

Notes:

[23] - 2-sided

Secondary: Change from baseline to End of Study Average in Total Asthma Symptoms

| | |
|------------------------|---|
| End point title | Change from baseline to End of Study Average in Total Asthma Symptoms |
| End point description: | End of study average is defined as the average of available records from 7 days before up to and including the day prior to withdrawal from study or Week 12, minus the baseline measurement at randomization, for patients who remain in the study (irrespective of whether IP has been discontinued). |
| End point type | Secondary |
| End point timeframe: | Week 12 |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--------------------------------------|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 70 | 72 | 73 | |
| Units: Asthma symptom scores | | | | |
| arithmetic mean (standard deviation) | -0.5 (± 0.73) | -0.6 (± 0.73) | -0.4 (± 0.55) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to End of Study Average in % of night time awakenings due to asthma symptoms

| | |
|-----------------|--|
| End point title | Change from baseline to End of Study Average in % of night |
|-----------------|--|

End point description:

End of study average is defined as the percentage of nighttime awakenings due to asthma symptoms from 6 days before up to and additionally including the morning of withdrawal from study or Week 12, minus the baseline measurement at randomization, for patients who remain in the study (irrespective of whether IP has been discontinued).

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

End point timeframe:

Week 12

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--------------------------------------|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 79 | 85 | 82 | |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | -14 (± 29.15) | -17.3 (± 33.16) | -13 (± 21.87) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to End of Study Average in Total daily reliever medication

| | |
|-----------------|---|
| End point title | Change from baseline to End of Study Average in Total daily reliever medication |
|-----------------|---|

End point description:

End of study average is defined as the average of available records from 7 days before up to and including the day prior to withdrawal from study or Week 12, minus the baseline measurement at randomization, for patients who remain in the study (irrespective of whether IP has been discontinued).

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

End point timeframe:

Week 12

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 70 | 72 | 73 | |
| Units: Number of reliever medication use | | | | |
| arithmetic mean (standard deviation) | -0.7 (± 1.75) | -1.1 (± 2.37) | -0.7 (± 1.37) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Study Period Average in Overall PAQLQ Score

| | |
|--|---|
| End point title | Change from baseline to Study Period Average in Overall PAQLQ Score |
| End point description: Study period average is defined as the average of the post-baseline values during the study taken after first dose of investigational product up to and including withdrawal from study or Week 12, minus the baseline assessment at randomization, for patients who remain in the study (irrespective of whether IP has been discontinued). | |
| End point type | Secondary |
| End point timeframe: Randomisation up to week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|--|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 79 | 80 | 82 | |
| Units: PAQLQ Scores | | | | |
| least squares mean (confidence interval 95%) | 0.46 (0.3 to 0.62) | 0.53 (0.38 to 0.69) | 0.62 (0.47 to 0.78) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Overall PAQLQ score, study period average |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Budesonide pMDI 80 ug |
| Number of subjects included in analysis | 161 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.098 ^[24] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.36 |
| upper limit | 0.03 |

Notes:

[24] - 2-sided

| | |
|----------------------------|---|
| Statistical analysis title | Overall PAQLQ score, study period average |
| Comparison groups | Budesonide pMDI 80 ug v Symbicort pMDI 80/2.25 ug |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 162 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.367 ^[25] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.29 |
| upper limit | 0.11 |

Notes:

[25] - 2-sided

| | |
|---|--|
| Statistical analysis title | Overall PAQLQ score, study period average |
| Comparison groups | Symbicort pMDI 80/4.5 ug v Symbicort pMDI 80/2.25 ug |
| Number of subjects included in analysis | 159 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.449 ^[26] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.27 |
| upper limit | 0.12 |

Notes:

[26] - 2-sided

Secondary: Number of patients with an asthma exacerbation during study

| | |
|---|---|
| End point title | Number of patients with an asthma exacerbation during study |
| End point description: Number of patients that experienced an asthma exacerbation that required either emergency room treatment, hospitalization, systemic steroids, or an increase in, or additional asthma maintenance medication, during the study. | |
| End point type | Secondary |
| End point timeframe: Randomisation up to Week 12 | |

| End point values | Symbicort pMDI 80/4.5 ug | Symbicort pMDI 80/2.25 ug | Budesonide pMDI 80 ug | |
|-----------------------------|--------------------------------|---------------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 90 | 93 | 90 | |
| Units: Participants | 9 | 12 | 12 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 weeks

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Symbicort pMDI 80/4.5 ug |
|-----------------------|--------------------------|

Reporting group description:

Symbicort pMDI 80/4.5 ug x 2 BID

| | |
|-----------------------|-----------------------|
| Reporting group title | Budesonide pMDI 80 ug |
|-----------------------|-----------------------|

Reporting group description:

Budesonide pMDI 80 ug x 2 BID

| | |
|-----------------------|---------------------------|
| Reporting group title | Symbicort pMDI 80/2.25 ug |
|-----------------------|---------------------------|

Reporting group description:

Symbicort pMDI 80/2.25 ug x 2 BID

| Serious adverse events | Symbicort pMDI 80/4.5 ug | Budesonide pMDI 80 ug | Symbicort pMDI 80/2.25 ug |
|---|--------------------------|-----------------------|---------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 90 (0.00%) | 2 / 90 (2.22%) | 0 / 93 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute lymphocytic leukaemia | | | |
| subjects affected / exposed | 0 / 90 (0.00%) | 1 / 90 (1.11%) | 0 / 93 (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 / 90 (0.00%) | 1 / 90 (1.11%) | 0 / 93 (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: 2 %

| Non-serious adverse events | Symbicort pMDI 80/4.5 ug | Budesonide pMDI 80 ug | Symbicort pMDI 80/2.25 ug |
|--|-----------------------------|--------------------------|------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 90 (46.67%) | 40 / 90 (44.44%) | 41 / 93 (44.09%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 90 (4.44%) | 0 / 90 (0.00%) | 4 / 93 (4.30%) |
| occurrences (all) | 4 | 0 | 4 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 90 (4.44%) | 4 / 90 (4.44%) | 4 / 93 (4.30%) |
| occurrences (all) | 4 | 4 | 4 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 2 / 90 (2.22%) | 0 / 90 (0.00%) | 0 / 93 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 90 (2.22%) | 0 / 90 (0.00%) | 3 / 93 (3.23%) |
| occurrences (all) | 2 | 0 | 3 |
| Nausea | | | |
| subjects affected / exposed | 0 / 90 (0.00%) | 2 / 90 (2.22%) | 0 / 93 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 7 / 90 (7.78%) | 10 / 90 (11.11%) | 11 / 93 (11.83%) |
| occurrences (all) | 7 | 10 | 11 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 3 / 90 (3.33%) | 4 / 90 (4.44%) | 3 / 93 (3.23%) |
| occurrences (all) | 3 | 5 | 3 |
| Cough | | | |
| subjects affected / exposed | 1 / 90 (1.11%) | 4 / 90 (4.44%) | 4 / 93 (4.30%) |
| occurrences (all) | 1 | 5 | 4 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 90 (1.11%) | 1 / 90 (1.11%) | 2 / 93 (2.15%) |
| occurrences (all) | 1 | 1 | 2 |
| Nasal congestion | | | |

| | | | |
|-----------------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 2 / 90 (2.22%) | 2 / 90 (2.22%) | 0 / 93 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 90 (2.22%) | 1 / 90 (1.11%) | 0 / 93 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 1 / 90 (1.11%) | 2 / 90 (2.22%) | 0 / 93 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 90 (0.00%) | 0 / 90 (0.00%) | 2 / 93 (2.15%) |
| occurrences (all) | 0 | 0 | 2 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 9 / 90 (10.00%) | 4 / 90 (4.44%) | 12 / 93 (12.90%) |
| occurrences (all) | 9 | 4 | 14 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 90 (4.44%) | 5 / 90 (5.56%) | 2 / 93 (2.15%) |
| occurrences (all) | 4 | 6 | 2 |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 90 (5.56%) | 1 / 90 (1.11%) | 3 / 93 (3.23%) |
| occurrences (all) | 5 | 1 | 4 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 90 (2.22%) | 1 / 90 (1.11%) | 1 / 93 (1.08%) |
| occurrences (all) | 2 | 1 | 1 |
| Influenza | | | |
| subjects affected / exposed | 1 / 90 (1.11%) | 0 / 90 (0.00%) | 2 / 93 (2.15%) |
| occurrences (all) | 1 | 0 | 2 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 90 (0.00%) | 1 / 90 (1.11%) | 2 / 93 (2.15%) |
| occurrences (all) | 0 | 1 | 2 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 90 (1.11%) | 2 / 90 (2.22%) | 0 / 93 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 90 (3.33%) | 2 / 90 (2.22%) | 2 / 93 (2.15%) |
| occurrences (all) | 3 | 2 | 2 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Viral upper respiratory tract subjects affected / exposed occurrences (all) | 0 / 90 (0.00%) 0 | 2 / 90 (2.22%) 2 | 1 / 93 (1.08%) 1 |
|---|---------------------|---------------------|---------------------|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 December 2014 | The primary analysis was revised to include all clinic FEV1 data from all patients, regardless of discontinuation of IP. Text was added to clarify a negative urine pregnancy test result should be obtained (where appropriate) prior to certain procedures at Visit 2 and prior to administration of IP at all other visits. For patients who meet pre-defined asthma worsening criteria, contact by the site within 24 to 48 hours was made mandatory, but the necessity of a clinic visit was changed to be at the discretion of the investigator. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported