# Clinical trial results:
# A Randomised Double-Blind, Double-Dummy, Placebo-Controlled, Stratified, Parallel-Group, Multicentre, Dose Ranging Study to Evaluate the Efficacy and Safety of GSK2190915 Tablets Administered Once Daily, Fluticasone Propionate Inhalation Powder 100mcg Twice Daily and Montelukast 10mg Once Daily compared with Placebo for 8 Weeks in Adolescent and Adult Subjects with Persistent Asthma while Treated with Short Acting Beta2-agonist

## Summary

| | |
|---|---|
| EudraCT number | 2010-019095-70 |
| Trial protocol | RO BG |
| Global end of trial date | 06 October 2011 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 27 April 2016 |
| First version publication date | 22 July 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | LPA112186 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01147744 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

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 | 18 November 2011 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 October 2011 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy, dose response and safety of four doses of GSK 2190915 (10mg, 30mg, 100mg and 300mg)

Protection of trial subjects:

A protocol amendment was issued restricting the study to females only following a finding from an interim histopathological assessment of the male reproductive tract from ongoing 6 month rat and 9 month dog toxicology studies. These findings related to testicular toxicity at high exposures of GSK2190915, the clinical significance of which was uncertain.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 28 June 2010 |
| 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 | Poland: 96 |
| Country: Number of subjects enrolled | Romania: 53 |
| Country: Number of subjects enrolled | Bulgaria: 105 |
| Country: Number of subjects enrolled | Japan: 84 |
| Country: Number of subjects enrolled | Ukraine: 186 |
| Country: Number of subjects enrolled | United States: 176 |
| Worldwide total number of subjects | 700 |
| EEA total number of subjects | 254 |

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) | 48 |
| Adults (18-64 years) | 606 |
| From 65 to 84 years | 46 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants (par.) were screened (Visit 1) for eligibility, which included reversibility testing. Following screening and a 14-days Run-in Period, par. who met the eligibility criteria for randomization to study treatment at Visit 3 were randomy assigned to receive one of seven double-blind treatments for 8 weeks.

### 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** | Placebo |

Arm description:

Participants received two tablets of placebo orally plus one dose of fluticasone propionate (FP) matching placebo twice daily (BID) via dry powder inhaler (DPI) in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally once daily (QD) in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received two tablets of placebo orally plus one dose of fluticasone propionate (FP) matching placebo twice daily (BID) via dry powder inhaler (DPI) in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally once daily (QD) in evening for the 8-Weeks.

| | |
|---|---|
| **Arm title** | GSK2190915, 10 mg, QD |

Arm description:

Participants received one tablet of 10 milligrams (mg) GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK2190915 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg (1 tablet once daily morning)

| | |
|---|---|
| **Arm title** | GSK2190915, 30 mg, QD |

Arm description:

Participants received one tablet of 30 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via

DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK2190915 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30 mg (1 tablet once daily morning)

| | |
|---|---|
| **Arm title** | GSK2190915, 100 mg, QD |

Arm description:

Participants received one tablet of 100 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK2190915 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg (1 tablet once daily morning)

| | |
|---|---|
| **Arm title** | GSK2190915, 300 mg, QD |

Arm description:

Participants received one tablet of 100 mg GSK2190915 and one tablet of 200 mg GSK 2190915 orally QD plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo BID via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK2190915 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg  (2 tablets once daily morning)

| | |
|---|---|
| **Arm title** | FP, 100 µg, BID |

Arm description:

Participants received one dose of FP 100 microgram (µg) BID via DPI plus two tablets of placebo in morning and another dose of FP 100 µg via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Fluticasone propionate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Inhalation use |

Dosage and administration details:

200 µg (100 µg inhaled morning and evening)

| | |
|---|---|
| **Arm title** | Montelukast, 10 mg, QD |

Arm description:

Participants received two tablets of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast 10 mg orally

QD in evening for the 8-Weeks.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Montelukast |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg (1 capsule once daily evening)

| **Number of subjects in period 1** | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD |
|---|---|---|---|
| Started | 100 | 99 | 100 |
| Completed | 71 | 76 | 82 |
| Not completed | 29 | 23 | 18 |
| Consent withdrawn by subject | 8 | 4 | 2 |
| Physician decision | - | 1 | 1 |
| Met Protocol-defined Stopping Criteria | 1 | - | - |
| Adverse event, non-fatal | 1 | 2 | 3 |
| Sponsor decision to amend protocol | 7 | 4 | 2 |
| Lost to follow-up | - | 1 | - |
| Lack of efficacy | 11 | 11 | 9 |
| Protocol deviation | 1 | - | 1 |

| **Number of subjects in period 1** | GSK2190915, 100 mg, QD | GSK2190915, 300 mg, QD | FP, 100 µg, BID |
|---|---|---|---|
| Started | 100 | 101 | 103 |
| Completed | 82 | 76 | 83 |
| Not completed | 18 | 25 | 20 |
| Consent withdrawn by subject | 2 | 2 | 5 |
| Physician decision | - | - | - |
| Met Protocol-defined Stopping Criteria | - | - | 1 |
| Adverse event, non-fatal | - | 2 | 1 |
| Sponsor decision to amend protocol | 5 | 7 | 2 |
| Lost to follow-up | - | - | - |
| Lack of efficacy | 11 | 13 | 8 |
| Protocol deviation | - | 1 | 3 |

| **Number of subjects in period 1** | Montelukast, 10 mg, QD |
|---|---|
| Started | 97 |
| Completed | 78 |
| Not completed | 19 |

| | |
|---|---|
| Consent withdrawn by subject | 2 |
| Physician decision | 1 |
| Met Protocol-defined Stopping Criteria | - |
| Adverse event, non-fatal | 2 |
| Sponsor decision to amend protocol | 6 |
| Lost to follow-up | - |
| Lack of efficacy | 7 |
| Protocol deviation | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received two tablets of placebo orally plus one dose of fluticasone propionate (FP) matching placebo twice daily (BID) via dry powder inhaler (DPI) in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally once daily (QD) in evening for the 8-Weeks. | |
| Reporting group title | GSK2190915, 10 mg, QD |
| Reporting group description: | |
| Participants received one tablet of 10 milligrams (mg) GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks. | |
| Reporting group title | GSK2190915, 30 mg, QD |
| Reporting group description: | |
| Participants received one tablet of 30 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks. | |
| Reporting group title | GSK2190915, 100 mg, QD |
| Reporting group description: | |
| Participants received one tablet of 100 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks. | |
| Reporting group title | GSK2190915, 300 mg, QD |
| Reporting group description: | |
| Participants received one tablet of 100 mg GSK2190915 and one tablet of 200 mg GSK 2190915 orally QD plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo BID via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks. | |
| Reporting group title | FP, 100 µg, BID |
| Reporting group description: | |
| Participants received one dose of FP 100 microgram (µg) BID via DPI plus two tablets of placebo in morning and another dose of FP 100 µg via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks. | |
| Reporting group title | Montelukast, 10 mg, QD |
| Reporting group description: | |
| Participants received two tablets of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast 10 mg orally QD in evening for the 8-Weeks. | |

| Reporting group values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD |
|---|---|---|---|
| Number of subjects | 100 | 99 | 100 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br>42.3<br>± 16.13 | <br><br>40<br>± 15.56 | <br><br>43.1<br>± 16.17 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 88 | 91 | 94 |

| | | | |
|---|---|---|---|
| Male | 12 | 8 | 6 |

| | | | |
|---|---|---|---|
| Race, Customized<br>Units: Subjects | | | |
| African American/African Heritage | 6 | 12 | 10 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian - Japanese Heritage | 12 | 12 | 12 |
| Asian - South East Asian Heritage | 0 | 1 | 0 |
| White - White/Caucasian/European Heritage | 82 | 74 | 78 |

| **Reporting group values** | GSK2190915, 100 mg, QD | GSK2190915, 300 mg, QD | FP, 100 µg, BID |
|---|---|---|---|
| Number of subjects | 100 | 101 | 103 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 42.2 | 42.2 | 41.5 |
| standard deviation | ± 14.63 | ± 14.15 | ± 15.16 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 92 | 93 | 97 |
| Male | 8 | 8 | 6 |
| Race, Customized<br>Units: Subjects | | | |
| African American/African Heritage | 9 | 9 | 7 |
| American Indian or Alaska Native | 2 | 1 | 1 |
| Asian - Japanese Heritage | 11 | 13 | 12 |
| Asian - South East Asian Heritage | 0 | 0 | 0 |
| White - White/Caucasian/European Heritage | 78 | 78 | 83 |

| **Reporting group values** | Montelukast, 10 mg, QD | Total | |
|---|---|---|---|
| Number of subjects | 97 | 700 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 44.3 | | |
| standard deviation | ± 14.97 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 89 | 644 | |
| Male | 8 | 56 | |
| Race, Customized<br>Units: Subjects | | | |
| African American/African Heritage | 9 | 62 | |
| American Indian or Alaska Native | 0 | 4 | |

| | | | |
|---|---|---|---|
| Asian - Japanese Heritage | 12 | 84 | |
| Asian - South East Asian Heritage | 0 | 1 | |
| White - White/Caucasian/European Heritage | 76 | 549 | |

## End points

### End points reporting groups

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

Reporting group description:

Participants received two tablets of placebo orally plus one dose of fluticasone propionate (FP) matching placebo twice daily (BID) via dry powder inhaler (DPI) in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally once daily (QD) in evening for the 8-Weeks.

| Reporting group title | GSK2190915, 10 mg, QD |
|---|---|

Reporting group description:

Participants received one tablet of 10 milligrams (mg) GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| Reporting group title | GSK2190915, 30 mg, QD |
|---|---|

Reporting group description:

Participants received one tablet of 30 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| Reporting group title | GSK2190915, 100 mg, QD |
|---|---|

Reporting group description:

Participants received one tablet of 100 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| Reporting group title | GSK2190915, 300 mg, QD |
|---|---|

Reporting group description:

Participants received one tablet of 100 mg GSK2190915 and one tablet of 200 mg GSK 2190915 orally QD plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo BID via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| Reporting group title | FP, 100 µg, BID |
|---|---|

Reporting group description:

Participants received one dose of FP 100 microgram (µg) BID via DPI plus two tablets of placebo in morning and another dose of FP 100 µg via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| Reporting group title | Montelukast, 10 mg, QD |
|---|---|

Reporting group description:

Participants received two tablets of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast 10 mg orally QD in evening for the 8-Weeks.

### Primary: Mean change from Baseline to the end of the 8-Week treatment period in trough FEV1

| End point title | Mean change from Baseline to the end of the 8-Week treatment period in trough FEV1 |
|---|---|

End point description:

Pulmonary function was measured by forced expiratory volume in one second (FEV1), defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 is defined as the morning (AM) pre-dose and pre-rescue bronchodilator FEV1 at the clinic visit. Baseline was the pre-dose value obtained at Visit 3. Change from Baseline was calculated as the end of Week 8 value minus the Baseline value. The analysis was performed using an analysis of covariance (ANCOVA) model with covariates of Baseline trough FEV1, age, gender, country and smoking status. The last observation carried forward (LOCF) method was used to impute missing data. Intent-to-Treat (ITT) Population is comprised of all par. randomized to treatment who received at least one dose of double-blind study medication.

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

End point timeframe:
Baseline and Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98[1] | 96[2] | 99[3] | 100[4] |
| Units: Liters | | | | |
| least squares mean (standard error) | 0.12 (± 0.04) | 0.18 (± 0.04) | 0.23 (± 0.04) | 0.19 (± 0.04) |

Notes:
[1] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.
[2] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.
[3] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.
[4] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 98[5] | 100[6] | 95[7] | |
| Units: Liters | | | | |
| least squares mean (standard error) | 0.19 (± 0.04) | 0.31 (± 0.04) | 0.19 (± 0.04) | |

Notes:
[5] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.
[6] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.
[7] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 194 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.326 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.056 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.06 |
| upper limit | 0.17 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |

| | |
|---|---|
| Number of subjects included in analysis | 197 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.066 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.104 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.01 |
| upper limit | 0.22 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.224 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.069 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.04 |
| upper limit | 0.18 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.271 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.062 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | 0.17 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|

| | |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.189 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.08 |
| upper limit | 0.3 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.22 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.04 |
| upper limit | 0.18 |

**Secondary: Mean change from Baseline in daily PM PEF averaged over the 8-Week treatment period**

| | |
|---|---|
| End point title | Mean change from Baseline in daily PM PEF averaged over the 8-Week treatment period |

End point description:

Peak expiratory flow (PEF) is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Change from Baseline was calculated as the value of the averaged PEF daily (pre-dose and pre-rescue bronchodilator) evening (PM) over the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, trough PM PEF, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[8] | 99[9] | 99[10] | 100[11] |
| Units: Liters per minute | | | | |
| least squares mean (standard error) | 8.01 (± 3.19) | 7.62 (± 3.19) | 9.37 (± 3.2) | 6.21 (± 3.17) |

Notes:

[8] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[9] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[10] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[11] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[12] | 101[13] | 97[14] | |
| Units: Liters per minute | | | | |
| least squares mean (standard error) | 10.33 (± 3.15) | 10.46 (± 3.16) | 8.53 (± 3.24) | |

Notes:

[12] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[13] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[14] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.932 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.385 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.25 |
| upper limit | 8.48 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.762 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.367 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | 10.23 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | GSK2190915, 100 mg, QD v Placebo |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.689 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.798 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.62 |
| upper limit | 7.03 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.605 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.321 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.49 |
| upper limit | 11.13 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.584 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.36 |
| upper limit | 11.28 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.907 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.529 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.4 |
| upper limit | 9.45 |

## Secondary: Mean change from Baseline in daily trough AM PEF averaged over the 8-Week treatment period

| End point title | Mean change from Baseline in daily trough AM PEF averaged over the 8-Week treatment period |
|---|---|

End point description:

The PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Trough AM PEF is defined as the AM pre-dose and pre-rescue bronchodilator at the clinic visit. Change from Baseline was calculated as the value of the averaged PEF daily (pre-dose and pre-rescue bronchodilator) AM over the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, trough AM PEF, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[15] | 99[16] | 99[17] | 100[18] |
| Units: Liters per minute | | | | |
| least squares mean (standard error) | 11.77 (± 3.28) | 13.23 (± 3.28) | 15.52 (± 3.29) | 8.72 (± 3.26) |

Notes:

[15] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[16] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[17] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[18] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[19] | 100[20] | 97[21] | |
| Units: Liters per minute | | | | |
| least squares mean (standard error) | 16.35 (± 3.24) | 15.25 (± 3.26) | 17.38 (± 3.32) | |

Notes:

[19] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[20] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[21] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.753 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.463 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.65 |
| upper limit | 10.58 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.419 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.75 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.36 |
| upper limit | 12.87 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.51 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3.046 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.12 |
| upper limit | 6.03 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.32 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 4.585 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.47 |
| upper limit | 13.64 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.452 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.484 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.61 |
| upper limit | 12.58 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.229 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 5.615 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.55 |
| upper limit | 14.78 |

## Secondary: Mean change from Baseline in the percentage of symptom-free days averaged over the 8-Week treatment period

| End point title | Mean change from Baseline in the percentage of symptom-free days averaged over the 8-Week treatment period |
|---|---|

End point description:

Asthma symptoms were recorded in a daily electronic diary (eDiary) by the par. every day in the evening at bedtime and before taking any rescue or study medication and before the assessment of the PEF measurement. Participant’s responses to evening assessments indicated no symptoms were considered to be symptom free. For participants, the symptom free days were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged of symptom-free days during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[22] | 99[23] | 99[24] | 100[25] |
| Units: Percentage of symptom-free days | | | | |
| least squares mean (standard error) | 13.98 (± 2.84) | 15.15 (± 2.84) | 18.54 (± 2.84) | 15.31 (± 2.82) |

Notes:

[22] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[23] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[24] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[25] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[26] | 101[27] | 97[28] | |
| Units: Percentage of symptom-free days | | | | |
| least squares mean (standard error) | 14.06 (± 2.81) | 22.18 (± 2.81) | 16.87 (± 2.87) | |

Notes:

[26] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[27] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[28] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.771 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.169 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.73 |
| upper limit | 9.07 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.257 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 4.56 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.33 |
| upper limit | 12.45 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.741 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.326 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.54 |
| upper limit | 9.19 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.983 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.083 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.76 |
| upper limit | 7.93 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.041 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 8.204 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.34 |
| upper limit | 16.07 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.475 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.891 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.05 |
| upper limit | 10.83 |

## Secondary: Mean change from Baseline in the percentage of symptom-free nights averaged over the 8-Week treatment period

| End point title | Mean change from Baseline in the percentage of symptom-free nights averaged over the 8-Week treatment period |
|---|---|

End point description:

Asthma symptoms were recorded in a daily eDairy by the par. every day in the morning upon rising and before taking any rescue or study medication and before the assessment of the PEF measurement. Participant's responses to the morning assessments indicated no symptoms were considered to be symptom free. For participants, the symptom free nights were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged of symptom-free nights during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[29] | 99[30] | 99[31] | 100[32] |
| Units: Percentage of symptom-free nights | | | | |
| least squares mean (standard error) | 13.99 (± 2.9) | 14.83 (± 2.9) | 16.71 (± 2.9) | 16.12 (± 2.88) |

Notes:

[29] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[30] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[31] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[32] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[33] | 100[34] | 97[35] | |
| Units: Percentage of symptom-free nights | | | | |
| least squares mean (standard error) | 12.21 (± 2.86) | 19.94 (± 2.88) | 19.39 (± 2.93) | |

Notes:

[33] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[34] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[35] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.838 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.837 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.22 |
| upper limit | 8.89 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.508 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.715 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.33 |
| upper limit | 10.76 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.603 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.124 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.9 |
| upper limit | 10.14 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.662 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.781 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.78 |
| upper limit | 6.22 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.146 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 5.949 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.08 |
| upper limit | 13.98 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.191 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 5.394 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.69 |
| upper limit | 13.48 |

## Secondary: Mean change from Baseline in the percentage of rescue-free days averaged over the 8-Week treatment period

| End point title | Mean change from Baseline in the percentage of rescue-free days averaged over the 8-Week treatment period |
|---|---|

End point description:

The number of inhalations of rescue salbutamol/albuterol inhalation aerosol used during the day and night was recorded by the par. in a eDiary. The time span during which the par. did not have to take any rescue medication (medication intended to relieve symptoms immediately) was considered to be a rescue-free period. For participants, the rescue-free days were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged of rescue-free days during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[36] | 99[37] | 99[38] | 100[39] |
| Units: Percentage of rescue-free days | | | | |
| least squares mean (standard error) | 16.8 (± 3.1) | 22.91 (± 3.1) | 20.91 (± 3.09) | 18.95 (± 3.08) |

Notes:

[36] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[37] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[38] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[39] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[40] | 101[41] | 97[42] | |
| Units: Percentage of rescue-free days | | | | |
| least squares mean (standard error) | 18.51 (± 3.06) | 26.39 (± 3.06) | 23.55 (± 3.13) | |

Notes:

[40] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[41] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[42] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.164 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 6.106 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 14.71 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.349 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 4.106 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.49 |
| upper limit | 12.7 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.623 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.148 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.42 |
| upper limit | 10.72 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.694 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.713 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.84 |
| upper limit | 10.26 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.028 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 9.592 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.03 |
| upper limit | 18.15 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.125 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 6.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.89 |
| upper limit | 15.38 |

## Secondary: Mean change from Baseline in the percentage of rescue-free nights averaged over the 8-Week treatment period

| End point title | Mean change from Baseline in the percentage of rescue-free nights averaged over the 8-Week treatment period |
|---|---|

End point description:

The number of inhalations of rescue salbutamol/albuterol inhalation aerosol used during the day and night was recorded by the par. in a eDiary. The time span during which the par. did not have to take any rescue medication (medication intended to relieve symptoms immediately) was considered to be a rescue-free period. For participants, the rescue-free nights were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged of rescue-free nights during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[43] | 99[44] | 99[45] | 100[46] |
| Units: Percentage of rescue-free nights | | | | |
| least squares mean (standard error) | 16.93 (± 3.04) | 19.28 (± 3.04) | 17.36 (± 3.03) | 19.63 (± 3.02) |

Notes:

[43] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[44] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[45] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[46] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[47] | 100[48] | 97[49] | |
| Units: Percentage of rescue-free nights | | | | |
| least squares mean (standard error) | 15.71 (± 3) | 24.42 (± 3.02) | 20.54 (± 3.07) | |

Notes:

[47] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[48] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[49] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.585 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.346 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.09 |
| upper limit | 10.78 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.431 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | 8.86 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.528 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.702 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.7 |
| upper limit | 11.11 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.776 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.218 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.6 |
| upper limit | 7.17 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.081 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 7.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.92 |
| upper limit | 15.9 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.403 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.611 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.87 |
| upper limit | 12.09 |

## Secondary: Mean change from Baseline in day-time asthma symptom score over the 8-Week treatment period

| End point title | Mean change from Baseline in day-time asthma symptom score over the 8-Week treatment period |
|---|---|

End point description:

Participants recorded their day-time asthma symptom score in the eDiary each PM at bedtime and before taking any rescue or study medication and before assessing the PEF measurement during the 8-Week treatment period. Day-time asthma symptom scores, as: 0=no asthma symptoms, 1=one episode of short-time asthma symptoms, 2=two or more episodes of short-time asthma symptoms, 3=asthma symptoms occurring during most part of daytime without interference with daily life activities, 4=asthma symptoms occurring during most part of daytime with interference with daily life activities, 5=severe asthma symptoms that disable working or perform normal daily activities. Change from Baseline was calculated as the averaged of day-time asthma symptom score during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[50] | 99[51] | 99[52] | 100[53] |
| Units: Day-time symptom scores on a scale | | | | |
| least squares mean (standard error) | -0.34 (± 0.06) | -0.34 (± 0.06) | -0.5 (± 0.06) | -0.36 (± 0.06) |

Notes:

[50] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[51] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[52] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[53] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[54] | 101[55] | 97[56] | |
| Units: Day-time symptom scores on a scale | | | | |
| least squares mean (standard error) | -0.34 (± 0.06) | -0.43 (± 0.06) | -0.41 (± 0.06) | |

Notes:

[54] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[55] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[56] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.951 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.005 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.17 |
| upper limit | 0.16 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |

| | |
|---|---|
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.043 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.166 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.33 |
| upper limit | -0.01 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.734 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.028 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.19 |
| upper limit | 0.13 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.972 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.003 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.16 |
| upper limit | 0.16 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|

| | |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.238 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.097 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.26 |
| upper limit | 0.06 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.36 |
| Method | ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | -0.075 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.24 |
| upper limit | 0.09 |

## Secondary: Mean change from Baseline in night-time asthma symptom score over the 8-Week treatment period

| End point title | Mean change from Baseline in night-time asthma symptom score over the 8-Week treatment period |
|---|---|

End point description:

Participants recorded their night-time asthma symptom score in the eDiary each AM upon rising and before taking any rescue or study medication and before assessing the PEF measurement during the 8-Week treatment period. Night-time asthma symptom scores, as: 0=no asthma symptoms, 1= one awakening or waking early due to asthma symptoms, 2= two or more awakenings due to asthma symptoms (including waking early), 3= asthma symptoms almost prevented the participant from sleeping, 4= severe asthma symptoms completely prevented from sleeping. Change from Baseline was calculated as the averaged of night-time asthma symptom score during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[57] | 99[58] | 99[59] | 100[60] |
| Units: Night-time symptom scores on a scale | | | | |
| least squares mean (standard error) | -0.23 (± 0.05) | -0.21 (± 0.05) | -0.33 (± 0.05) | -0.26 (± 0.05) |

Notes:

[57] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[58] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[59] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[60] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[61] | 100[62] | 97[63] | |
| Units: Night-time symptom scores on a scale | | | | |
| least squares mean (standard error) | -0.22 (± 0.05) | -0.29 (± 0.05) | -0.32 (± 0.05) | |

Notes:

[61] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[62] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[63] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.692 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.028 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.11 |
| upper limit | 0.17 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |

| | |
|---|---|
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.176 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.096 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.24 |
| upper limit | 0.04 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.768 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.021 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.16 |
| upper limit | 0.12 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.887 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.13 |
| upper limit | 0.15 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|

| | |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.471 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.051 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.19 |
| upper limit | 0.09 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.248 |
| Method | ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | -0.083 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.22 |
| upper limit | 0.06 |

**Secondary: Mean change from Baseline in day-time rescue SABA usage over the 8-Week treatment period**

| End point title | Mean change from Baseline in day-time rescue SABA usage over the 8-Week treatment period |
|---|---|

End point description:

The number of inhalations of rescue short acting beta2-agonist (SABA), salbutamol/albuterol inhalation aerosol used during the day and night was recorded by the par. in a eDiary. Participants who used salbutamol/albuterol inhalation aerosol at day-time were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged number of day-time salbutamol/albuterol inhalation aerosol used during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[64] | 99[65] | 99[66] | 100[67] |
| Units: Day-time number of inhalations | | | | |
| least squares mean (standard error) | -0.42 (± 0.07) | -0.55 (± 0.07) | -0.68 (± 0.07) | -0.5 (± 0.07) |

Notes:

[64] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[65] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[66] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[67] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[68] | 101[69] | 97[70] | |
| Units: Day-time number of inhalations | | | | |
| least squares mean (standard error) | -0.47 (± 0.07) | -0.67 (± 0.07) | -0.63 (± 0.07) | |

Notes:

[68] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[69] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[70] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.209 |
| Method | ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | -0.131 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.33 |
| upper limit | 0.07 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.011 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.264 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.47 |
| upper limit | -0.06 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.464 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.076 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.28 |
| upper limit | 0.13 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.662 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.045 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.25 |
| upper limit | 0.16 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.018 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.245 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.45 |
| upper limit | -0.04 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.047 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.207 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.41 |
| upper limit | 0 |

## Secondary: Mean change from Baseline in night-time rescue SABA usage over the 8-Week treatment period

| End point title | Mean change from Baseline in night-time rescue SABA usage over the 8-Week treatment period |
|---|---|

End point description:

The numbers of inhalations of rescue SABA, salbutamol/albuterol inhalation aerosol used during the day and night was recorded by the par. in a eDiary. Participants who used salbutamol/albuterol inhalation aerosol at night-time were assessed during the 8-Week treatment period. Change from Baseline was calculated as the averaged number of night-time salbutamol/albuterol inhalation aerosol used during the 8-Week treatment period minus the Baseline value (defined as the last 7 days prior to randomization of the par.). Analysis was performed using ANCOVA with covariates of Baseline, age, gender, country and smoking status.

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

End point timeframe:

From Baseline up to Week 8

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 99[71] | 99[72] | 99[73] | 100[74] |
| Units: Night-time number of inhalations | | | | |
| least squares mean (standard error) | -0.3 (± 0.07) | -0.4 (± 0.07) | -0.44 (± 0.07) | -0.42 (± 0.07) |

Notes:

[71] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[72] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[73] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[74] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[75] | 100[76] | 97[77] | |
| Units: Night-time number of inhalations | | | | |
| least squares mean (standard error) | -0.3 (± 0.07) | -0.47 (± 0.07) | -0.46 (± 0.07) | |

Notes:

[75] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[76] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

[77] - ITT Population. Only those par. with analyzable data at the indicated time point were assessed.

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.098 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.28 |
| upper limit | 0.09 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | GSK2190915, 30 mg, QD v Placebo |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.145 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.138 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.32 |
| upper limit | 0.05 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.19 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.123 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.31 |
| upper limit | 0.06 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.98 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.002 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.19 |
| upper limit | 0.18 |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |

| | |
|---|---|
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.07 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.171 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.36 |
| upper limit | 0.01 |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 196 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.095 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.158 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.34 |
| upper limit | 0.03 |

## Secondary: Number of participants who withdrew due to lack of efficacy during the 8-Week treatment period

| End point title | Number of participants who withdrew due to lack of efficacy during the 8-Week treatment period |
|---|---|

End point description:

The participants who met any of the following withdrawal criteria were considered to be withdrawn due to lack of efficacy: 1) Clinic FEV1 below stability limit calculated at Visit 3. 2) More than three days between two consecutive visits, PEF has fallen below stability limit calculated at Visit 3. 3) Use of 12 or more inhalations of SABA per day for more than two days between consecutive visits. 4) Asthma exacerbation defined as worsening requiring any treatment other than study medication or rescue medication. This included requiring the use of systemic or inhaled corticosteroids and /or emergency room visit or hospitalization for the treatment of asthma. The stability limit was calculated as best pre-salbutamol/albuterol FEV1 at Visit 3 x 80 percent (%).

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

End point timeframe:

8 Weeks

| End point values | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD | GSK2190915, 100 mg, QD |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 100[78] | 99[79] | 100[80] | 100[81] |
| Units: Participants | 11 | 11 | 9 | 11 |

Notes:

[78] - ITT Population

[79] - ITT Population

[80] - ITT Population

[81] - ITT Population

| End point values | GSK2190915, 300 mg, QD | FP, 100 µg, BID | Montelukast, 10 mg, QD | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 101[82] | 103[83] | 97[84] | |
| Units: Participants | 13 | 8 | 7 | |

Notes:

[82] - ITT Population

[83] - ITT Population

[84] - ITT Population

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 10 mg, QD |
| Number of subjects included in analysis | 199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Fisher exact |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 30 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.814 |
| Method | Fisher exact |

| Statistical analysis title | Statistical Analysis 3 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 100 mg, QD |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Fisher exact |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|
| Comparison groups | Placebo v GSK2190915, 300 mg, QD |
| Number of subjects included in analysis | 201 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.828 |
| Method | Fisher exact |

| **Statistical analysis title** | Statistical Analysis 5 |
|---|---|
| Comparison groups | Placebo v FP, 100 µg, BID |
| Number of subjects included in analysis | 203 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.477 |
| Method | Fisher exact |

| **Statistical analysis title** | Statistical Analysis 6 |
|---|---|
| Comparison groups | Placebo v Montelukast, 10 mg, QD |
| Number of subjects included in analysis | 197 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.46 |
| Method | Fisher exact |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of administration of the study drug until the follow-up contact (up to Week 9).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the ITT population, comprised of all participants who were randomized to treatment, and received at least one dose of double-blind study medication.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |

### Reporting groups

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

Reporting group description:

Participants received two tablets of placebo orally plus one dose of fluticasone propionate (FP) matching placebo twice daily (BID) via dry powder inhaler (DPI) in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally once daily (QD) in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | GSK2190915, 10 mg, QD |

Reporting group description:

Participants received one tablet of 10 milligrams (mg) GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | GSK2190915, 30 mg, QD |

Reporting group description:

Participants received one tablet of 30 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | GSK2190915, 100 mg, QD |

Reporting group description:

Participants received one tablet of 100 mg GSK2190915 orally QD and one tablet of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | GSK2190915, 300 mg, QD |

Reporting group description:

Participants received one tablet of 100 mg GSK2190915 and one tablet of 200 mg GSK2190915 orally QD plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo BID via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | FP, 100 µg, BID |

Reporting group description:

Participants received one dose of FP 100 microgram (µg) BID via DPI plus two tablets of placebo in morning and another dose of FP 100 µg via DPI plus one capsule of montelukast matching placebo orally QD in evening for the 8-Weeks.

| | |
|---|---|
| Reporting group title | Montelukast, 10 mg, QD |

Reporting group description:

Participants received two tablets of placebo orally plus one dose of FP matching placebo BID via DPI in morning and another dose of FP matching placebo via DPI plus one capsule of montelukast 10 mg orally QD in evening for the 8-Weeks.

| Serious adverse events | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 99 (1.01%) | 0 / 100 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Cartilage injury | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 99 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 99 (1.01%) | 0 / 100 (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 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 99 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | GSK2190915, 100 mg, QD | GSK2190915, 300 mg, QD | FP, 100 µg, BID |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 1 / 103 (0.97%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Cartilage injury | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 1 / 103 (0.97%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 103 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Montelukast, 10 mg, QD | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Cartilage injury | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 97 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Placebo | GSK2190915, 10 mg, QD | GSK2190915, 30 mg, QD |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 100 (10.00%) | 13 / 99 (13.13%) | 6 / 100 (6.00%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 7 / 99 (7.07%) | 2 / 100 (2.00%) |
| occurrences (all) | 3 | 7 | 2 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 6 / 99 (6.06%) | 3 / 100 (3.00%) |
| occurrences (all) | 5 | 6 | 3 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 99 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 2 | 0 | 1 |

| **Non-serious adverse events** | GSK2190915, 100 mg, QD | GSK2190915, 300 mg, QD | FP, 100 µg, BID |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | 9 / 101 (8.91%) | 14 / 103 (13.59%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 4 / 101 (3.96%) | 9 / 103 (8.74%) |
| occurrences (all) | 4 | 4 | 9 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 5 / 101 (4.95%) | 5 / 103 (4.85%) |
| occurrences (all) | 2 | 5 | 5 |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 0 / 101 (0.00%) | 0 / 103 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| **Non-serious adverse events** | Montelukast, 10 mg, QD | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 97 (15.46%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 97 (9.28%) | | |
| occurrences (all) | 9 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 13 October 2010 | The amendment restricted the study to females only following a finding from an interim histopathological assessment of the male reproductive tract from ongoing 6 month rat and 9 month dog toxicology studies. These findings related to testicular toxicity at high exposures of GSK2190915, the clinical significance of which was uncertain. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported