Clinical trial results:
A Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Five-Treatment, Four 6-Week Period Cross-Over, Multi-Center Study to Evaluate the Effect of Adding GSK2190915 100mg, GSK2190915 300mg, Montelukast 10mg or Placebo Tablets Once Daily or Salmeterol 50mcg Inhalation Powder Twice Daily to Fluticasone Propionate 100mcg Inhalation Powder Twice Daily in Uncontrolled Asthmatic Subjects >=12 Years of Age

Summary

EudraCT number	2010-019466-81
Trial protocol	Outside EU/EEA
Global end of trial date	25 October 2011

Results information

Result version number	v1 (current)
This version publication date	29 December 2016
First version publication date	29 December 2016

Trial information

Trial identification

Sponsor protocol code	114255

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 December 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to evaluate the efficacy and safety of adding GSK2190915 100mg, GSK2190915 300mg or placebo tablets administered once daily to FP 100mcg inhalation administered twice daily in uncontrolled asthmatic female subjects >=12 years of age over the course of 6 weeks treatment.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 September 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	United States: 341
Worldwide total number of subjects	341
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	41
Adults (18-64 years)	290
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 341 participants (par.) were screened, and 162 participants were randomized. A protocol amendment necessitated withdrawal of all male participants and further enrollment of female participants only.

Pre-assignment

Screening details:

Par. meeting screening criteria, self-administered open-label fluticasone propionate 100 micrograms (µg) twice daily for 14-28 days. Eligible par. were assigned to 1 of 10 treatment sequences, receiving 4 of 5 double-blind treatments. Par. aged 12-14 years did not receive montelukast. Rescue medication (albuterol inhalation) was provided.

Period 1

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

Arms

Arm title	All Treatments Combined

Arm description:

In a total of 4 treatment periods (each of 6 weeks - the first 3 weeks considered as active washout), participants received 4 of the 5 possible treatments (A/B/C/D/E) in a double-blind double-dummy, cross-over manner. Fluticasone propionate (FP) 100 µg oral inhalation was a part of each treatment. Added regimen were, A: GSK2190915 100 milligrams (mg) once daily (OD), B: GSK2190915 300 mg OD, C: montelukast 10 mg OD, D: placebo twice daily (BID), E: salmeterol 50 µg and placebo BID. Albuterol aerosol was provided as a rescue inhalation.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Oral use

Dosage and administration details:

One inhalation of fluticasone propionate 100 µg BID for 6 weeks

Investigational medicinal product name	GSK2190915 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of GSK2190915 100 mg every morning for 6 weeks

Investigational medicinal product name	Fluticasone Propionate/Salmeterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Oral use

Dosage and administration details:

One inhalation of fluticasone propionate/salmeterol 100 µg /50 µg BID for 6 weeks

Investigational medicinal product name	GSK2190915 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of GSK2190915 200 mg every morning for 6 weeks

Investigational medicinal product name	Placebo to match GSK2190915
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets every morning for 6 weeks

Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule of montelukast 10 mg every evening for 6 weeks

Investigational medicinal product name	Placebo to match Montelukast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule every evening for 6 weeks

Number of subjects in period 1[1]	All Treatments Combined
Started	162
Completed	93
Not completed	69
Physician decision	3
Consent withdrawn by subject	9
Adverse event, non-fatal	1
other Sponsor Decision (Protocol Amendme	11
Lost to follow-up	3
Lack of efficacy	36
Protocol deviation	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 341 participants were screened and 162 participants were randomized.

Baseline characteristics

Reporting groups	
Reporting group title	All Treatments Combined

Reporting group description:

In a total of 4 treatment periods (each of 6 weeks - the first 3 weeks considered as active washout), participants received 4 of the 5 possible treatments (A/B/C/D/E) in a double-blind double-dummy, cross-over manner. Fluticasone propionate (FP) 100 µg oral inhalation was a part of each treatment. Added regimen were, A: GSK2190915 100 milligrams (mg) once daily (OD), B: GSK2190915 300 mg OD, C: montelukast 10 mg OD, D: placebo twice daily (BID), E: salmeterol 50 µg and placebo BID. Albuterol aerosol was provided as a rescue inhalation.

Reporting group values	All Treatments Combined	Total	
Number of subjects	162	162	
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	36.8		
standard deviation	± 14.43	-	
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	151	151	
Male	11	11	
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	42	42	
American Indian or Alaska Native	1	1	
Asian - Central/South Asian Heritage	1	1	
White - White/Caucasian/European Heritage	115	115	
Mixed Race	2	2	
Missing	1	1	

End points

End points reporting groups

Reporting group title	All Treatments Combined

Reporting group description:

In a total of 4 treatment periods (each of 6 weeks - the first 3 weeks considered as active washout), participants received 4 of the 5 possible treatments (A/B/C/D/E) in a double-blind double-dummy, cross-over manner. Fluticasone propionate (FP) 100 µg oral inhalation was a part of each treatment. Added regimen were, A: GSK2190915 100 milligrams (mg) once daily (OD), B: GSK2190915 300 mg OD, C: montelukast 10 mg OD, D: placebo twice daily (BID), E: salmeterol 50 µg and placebo BID. Albuterol aerosol was provided as a rescue inhalation.

Subject analysis set title	FP + Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received FP 100 µg oral inhalation twice daily (BID) for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Placebo administered every morning (AM) was added to the dosing regimen. Blinding was maintained by administration of a montelukast-matching placebo capsule every evening (PM). Albuterol aerosol was provided as a rescue inhalation.

Subject analysis set title	FP + GSK2190915 100 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. GSK2190915 100 mg AM was added to the dosing regimen. Blinding was maintained by PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Subject analysis set title	FP + GSK2190915 300 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. GSK2190915 300 mg AM was added to the dosing regimen. Blinding was maintained by PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Subject analysis set title	FP + Montelukast
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Montelukast 10 mg capsule administered PM was added to the dosing regimen. Blinding was maintained by AM administration of GSK2190915-matching placebo tablets. Albuterol aerosol was provided as a rescue inhalation.

Subject analysis set title	FP / Salmeterol
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received a combination of FP 100 µg and salmeterol 50 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Blinding was maintained by AM administration of GSK2190915-matching placebo tablets and PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Primary: Trough (AM pre-dose and pre-rescue bronchodilator) forced expiratory volume in 1 second (FEV1) at the end of the 6-week treatment period

End point title	Trough (AM pre-dose and pre-rescue bronchodilator) forced expiratory volume in 1 second (FEV1) at the end of the 6-week treatment period

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. FEV1 was measured electronically using spirometry, prior to study medication and any rescue albuterol (bronchodilator) use. At the end of the 6-week treatment period, FEV1 was measured approximately 24 hours after the participant’s last morning dose of study medication and approximately 12 hours after the evening dose of study medication. Trough FEV1 was analyzed using

mixed effect analysis of covariance (ANCOVA) model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effect of participant. Intent-to-Treat Population (ITT) is defined as all participants who were randomized and received at least one dose of study drug.

End point type	Primary

End point timeframe:

End of Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[1]	92[2]	93[3]	94[4]
Units: Liters (L)				
least squares mean (standard error)	2.36 (± 0.03)	2.39 (± 0.03)	2.4 (± 0.03)	2.42 (± 0.03)

Notes:

[1] - ITT Population

[2] - ITT Population

[3] - ITT Population

[4] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	93[5]			
Units: Liters (L)				
least squares mean (standard error)	2.43 (± 0.03)			

Notes:

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + GSK2190915 100 mg v FP + Placebo
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.268
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.026
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.07

Statistical analysis title	Statistical analysis 2

Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.08
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.042
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.09

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.056
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.1

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.12

Secondary: Daily trough (morning pre-dose and pre-rescue bronchodilator) morning peak expiratory flow (PEF) averaged over the last 3 weeks of the 6-week treatment period

End point title	Daily trough (morning pre-dose and pre-rescue bronchodilator) morning peak expiratory flow (PEF) averaged over the last 3 weeks of the 6-week treatment period

End point description:

The PEF is a measure of lung function and measures how fast a person can breathe out. Trough PEF was measured every morning prior to study medication dose and any rescue albuterol (bronchodilator) use. Participants recorded PEF in a daily electronic diary (eDiary). Daily trough morning PEF was averaged over the last 3 weeks of the 6-week treatment period, and analyzed using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[6]	92[7]	92[8]	93[9]
Units: Liters/minute (L/min)				
least squares mean (standard error)	349.19 (± 4.08)	350.14 (± 4.06)	354.96 (± 4.07)	354.17 (± 4.05)

Notes:

[6] - ITT Population

[7] - ITT Population

[8] - ITT Population

[9] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[10]			
Units: Liters/minute (L/min)				
least squares mean (standard error)	361.33 (± 4.05)			

Notes:

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.751
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.946

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.91
upper limit	6.81

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.049
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.771
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	11.51

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.123
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.983
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	11.32

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	12.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.93
upper limit	18.35

Secondary: Daily evening PEF averaged over the last 3 weeks of the 6-week treatment period

End point title	Daily evening PEF averaged over the last 3 weeks of the 6-week treatment period

End point description:

The PEF is a measure of lung function and measures how fast a person can breathe out. PEF was measured every evening prior to study medication dose and any rescue albuterol (bronchodilator) use. Participants recorded PEF in a daily eDiary. Daily evening PEF was averaged over the last 3 weeks of the 6-week treatment period, and analyzed using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[11]	92[12]	92[13]	93[14]
Units: L/min				
least squares mean (standard error)	354.06 (± 4.03)	355.71 (± 4.02)	359.16 (± 4.03)	358.88 (± 4.01)

Notes:

[11] - ITT Population

[12] - ITT Population

[13] - ITT Population

[14] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[15]			
Units: L/min				
least squares mean (standard error)	364.35 (± 4)			

Notes:
[15] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.563
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.651
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.97
upper limit	7.27

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.072
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	10.67

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.126
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.822
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.37
upper limit	11.02

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	10.292
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.21
upper limit	16.38

Secondary: Daily (average of morning and evening) PEF averaged over the last 3 weeks of the 6 -week treatment period between GSK2190915 and montelukast groups

End point title	Daily (average of morning and evening) PEF averaged over the last 3 weeks of the 6 -week treatment period between GSK2190915 and montelukast groups

End point description:

The PEF is a measure of lung function and measures how fast a person can breathe out. PEF was measured every morning and evening prior to study medication dose and any rescue albuterol (bronchodilator) use. Participants recorded PEF in a daily eDiary. Daily average of morning and evening PEF was averaged over the last 3 weeks of the 6-week treatment period, and analyzed using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant. This outcome measure explored the efficacy between GSK2190915 and montelukast due to the dosing time difference.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	93[16]	92[17]	93[18]	
Units: L/min				
least squares mean (standard error)	352.37 (± 3.9)	356.16 (± 3.91)	356.52 (± 3.9)	

Notes:

[16] - ITT Population

[17] - ITT Population

[18] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + GSK2190915 100 mg v FP + Montelukast
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4.154
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.36
upper limit	1.06

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + GSK2190915 300 mg v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.364
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.22
upper limit	5.5

Secondary: Daily asthma symptom score averaged over the last 3 weeks of the 6-week treatment period

End point title	Daily asthma symptom score averaged over the last 3 weeks of the 6-week treatment period

End point description:

Daytime and night time asthma symptoms were recorded every evening at bedtime and every morning upon rising, respectively, before taking any rescue or study medication and before assessing the PEF. Symptoms were recorded on scales ranging from ‘0’ (implying no symptoms) to either 5 (for daytime

symptoms) or 4 (for night time symptoms) (implying severe symptoms). Participants recorded the symptoms in a daily eDiary. 24-hour period asthma symptom scores were averaged over the last 3 weeks of the 6-week treatment period, and analyzed using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[19]	90[20]	92[21]	93[22]
Units: Score on a scale				
least squares mean (standard error)	2.26 (± 0.12)	2.26 (± 0.12)	2.15 (± 0.12)	2.22 (± 0.12)

Notes:

[19] - ITT Population

[20] - ITT Population

[21] - ITT Population

[22] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[23]			
Units: Score on a scale				
least squares mean (standard error)	2.25 (± 0.12)			

Notes:

[23] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.957
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.17

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.213
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.108
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.06

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.647
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.12

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.894
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.011
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.15

Secondary: Daily rescue short-acting beta2-agonist (SABA) use averaged over the last 3 weeks of the 6-week treatment period

End point title	Daily rescue short-acting beta2-agonist (SABA) use averaged over the last 3 weeks of the 6-week treatment period

End point description:

A SABA (albuterol) was provided to participants as a rescue medication, to use as needed for symptomatic relief of asthma symptoms. Participants were required to record their albuterol use in the morning and in the evening. Participants recorded the number of inhalations of rescue medication in a daily eDiary. The daily rescue SABA use was averaged over the last 3 weeks of the 6-week treatment period, and analyzed using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[24]	90[25]	92[26]	93[27]
Units: Number of inhalations				
least squares mean (standard error)	2.17 (± 0.13)	2.14 (± 0.13)	2.03 (± 0.13)	2.09 (± 0.13)

Notes:

[24] - ITT Population

[25] - ITT Population

[26] - ITT Population

[27] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[28]			
Units: Number of inhalations				
least squares mean (standard error)	2.08 (± 0.13)			

Notes:

[28] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.811
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.025

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.18

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.133
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.07

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.415
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.11

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.358
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.1

Secondary: Percentage of symptom-free days during the last 3 weeks of the 6-week treatment period

End point title	Percentage of symptom-free days during the last 3 weeks of the 6-week treatment period

End point description:

Daytime asthma symptoms were recorded every evening at bedtime, before taking any rescue or study medication and before assessing the PEF. Symptoms were recorded on a 6-point scale ranging from '0' (implying no symptoms) to 5 (implying severe symptoms). Participants recorded the symptoms in a daily eDiary. The number of days when symptoms were not experienced ("symptom-free days") during the last 3 weeks of the 6-week treatment period were counted, and percentage calculated by dividing by 21 and multiplying by 100. Analysis was done using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[29]	92[30]	92[31]	93[32]
Units: Percentage of days				
least squares mean (standard error)	30.84 (± 3.04)	33.51 (± 3.02)	36.14 (± 3.03)	34.88 (± 3.01)

Notes:

[29] - ITT Population

[30] - ITT Population

[31] - ITT Population

[32] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[33]			
Units: Percentage of days				
least squares mean (standard error)	35.45 (± 3.02)			

Notes:
[33] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.285
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.666
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	7.57

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.035
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	10.22

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.09
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	8.7

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.047
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.602
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	9.14

Secondary: Percentage of symptom-free nights during the last 3 weeks of the 6 week treatment period

End point title	Percentage of symptom-free nights during the last 3 weeks of the 6 week treatment period

End point description:

Night time asthma symptoms were recorded every morning upon rising, before taking any rescue or study medication and before assessing the PEF. Symptoms were recorded on a 5-point scale ranging from '0' (implying no symptoms) to 4 (implying severe symptoms). Participants recorded the symptoms in a daily eDiary. The number of nights when symptoms were not experienced ("symptom-free nights") during the last 3 weeks of the 6-week treatment period were counted, and percentage calculated by dividing by 21 and multiplying by 100. Analysis was done using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[34]	92[35]	92[36]	93[37]
Units: Percentage of nights				
least squares mean (standard error)	37.21 (± 2.87)	38.22 (± 2.85)	40.55 (± 2.85)	37.7 (± 2.84)

Notes:

[34] - ITT Population

[35] - ITT Population

[36] - ITT Population

[37] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[38]			
Units: Percentage of nights				
least squares mean (standard error)	38.47 (± 2.85)			

Notes:

[38] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.668
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	5.67

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.156
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.349

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.29
upper limit	7.98

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.822
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.496
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	4.82

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.555
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.94
upper limit	5.46

Secondary: Percentage of rescue-free days during the last 3 weeks of the 6-week treatment period

End point title	Percentage of rescue-free days during the last 3 weeks of the 6-week treatment period

End point description:

Albuterol was provided as a rescue medication, and participants were required to record rescue medication use in the morning and in the evening. Participants recorded the number of inhalations of rescue medication in a daily eDiary. The number of days when rescue medication was not used (“rescue-free days”) during the last 3 weeks of the 6-week treatment period were counted, and

percentage calculated by dividing by 21 and multiplying by 100. Analysis was done using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[39]	92[40]	92[41]	93[42]
Units: Percentage of days				
least squares mean (standard error)	40.44 (± 3.05)	42.43 (± 3.03)	42.59 (± 3.04)	42.77 (± 3.02)

Notes:

[39] - ITT Population

[40] - ITT Population

[41] - ITT Population

[42] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[43]			
Units: Percentage of days				
least squares mean (standard error)	41.96 (± 3.03)			

Notes:

[43] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.367
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.992
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.35
upper limit	6.33

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg

Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.332
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.147
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	6.49

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.277
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.331
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	6.55

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.467
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.521
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.59
upper limit	5.63

Secondary: Percentage of rescue-free nights during the last 3 weeks of the 6-week

treatment period	
End point title	Percentage of rescue-free nights during the last 3 weeks of the 6-week treatment period

End point description:

Albuterol was provided as a rescue medication, and participants were required to record rescue medication use in the morning and in the evening. Participants recorded the number of inhalations of rescue medication in a daily eDiary. The number of nights when rescue medication was not used ("rescue-free nights") during the last 3 weeks of the 6-week treatment period were counted, and percentage calculated by dividing by 21 and multiplying by 100. Analysis was done using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[44]	92[45]	92[46]	93[47]
Units: Percentage of nights				
least squares mean (standard error)	45.12 (± 2.87)	45.69 (± 2.85)	48.79 (± 2.86)	45.32 (± 2.85)

Notes:

[44] - ITT Population

[45] - ITT Population

[46] - ITT Population

[47] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[48]			
Units: Percentage of nights				
least squares mean (standard error)	43.98 (± 2.85)			

Notes:

[48] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.789
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.575

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.65
upper limit	4.8

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.087
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.669
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	7.87

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.923
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.84
upper limit	4.24

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.571
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.137
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.08
upper limit	2.81

Secondary: Percentage of nights without awakenings due to asthma during the last 3 weeks of the 6-week treatment period

End point title	Percentage of nights without awakenings due to asthma during the last 3 weeks of the 6-week treatment period

End point description:

Night time asthma symptoms were recorded every morning upon rising, before taking any rescue or study medication and before assessing the PEF. Symptoms were recorded on a 5-point scale: 0 = no symptoms during the night, 1 = symptoms causing to wake once, 2 = symptoms causing to wake twice or more, 3 = symptoms causing to be awake most of the night, 4 = could not sleep due to severe symptoms. Participants recorded the symptoms in a daily eDiary. The number of nights with no awakenings due to asthma during the last 3 weeks of the 6-week treatment period were counted, and percentage calculated by dividing by 21 and multiplying by 100. Analysis was done using mixed effect ANCOVA model for treatment effects, incorporating fixed effects of baseline, period, age, center, smoking status, and random effects of participant.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	92[49]	92[50]	92[51]	93[52]
Units: Percentage of nights				
least squares mean (standard error)	37.21 (± 2.87)	38.22 (± 2.85)	40.55 (± 2.85)	37.7 (± 2.84)

Notes:

[49] - ITT Population

[50] - ITT Population

[51] - ITT Population

[52] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	95[53]			
Units: Percentage of nights				
least squares mean (standard error)	38.47 (± 2.85)			

Notes:
[53] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.668
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	5.67

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.156
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.349
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.29
upper limit	7.98

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.822
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.496
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	4.82

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.555
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.94
upper limit	5.46

Secondary: Number of participants withdrawn due to lack of efficacy during the last 3 weeks of the 6-week treatment period

End point title	Number of participants withdrawn due to lack of efficacy during the last 3 weeks of the 6-week treatment period

End point description:

Participants were withdrawn if they met any of the following three criteria for 'lack of efficacy': 1) Clinic FEV1 below the FEV1 'Stability Limit' value, 2) During any consecutive 7-day period, the participant experienced PEF fallen below the PEF 'Stability Limit' for more than 3 days, or if >= 12 inhalations per day of albuterol were used for more than 2 days, and 3) Ashtma exacerbation. The number of withdrawals due to lack of efficacy were summarized for each treatment and Fisher's Exact test was used for comparison with placebo add-on. Withdrawals occurring during active washout periods are not included.

End point type	Secondary

End point timeframe:

Week 4 to Week 6

End point values	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg	FP + Montelukast
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	104[54]	103[55]	96[56]	99[57]
Units: Number of participants	9	5	3	7

Notes:

[54] - ITT Population

[55] - ITT Population

[56] - ITT Population

[57] - ITT Population

End point values	FP / Salmeterol			
Subject group type	Subject analysis set			
Number of subjects analysed	104[58]			
Units: Number of participants	5			

Notes:

[58] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FP + Placebo v FP + GSK2190915 100 mg
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.408
Method	Fisher exact
Confidence interval	
level	95 %

Statistical analysis title	Statistical analysis 2
Comparison groups	FP + Placebo v FP + GSK2190915 300 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.138
Method	Fisher exact
Confidence interval	
level	95 %

Statistical analysis title	Statistical analysis 3
Comparison groups	FP + Placebo v FP + Montelukast

Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.797
Method	Fisher exact
Confidence interval	
level	95 %

Statistical analysis title	Statistical analysis 4
Comparison groups	FP + Placebo v FP / Salmeterol
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.408
Method	Fisher exact
Confidence interval	
level	95 %

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment adverse events (AE) and serious adverse events (SAE) were collected from the start of treatment until the follow-up contact (a maximum of 178 days).

Adverse event reporting additional description:

On-treatment AEs and SAEs are reported for the ITT Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	FP + Placebo

Reporting group description:

Participants received FP 100 µg oral inhalation twice daily (BID) for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Placebo administered every morning (AM) was added to the dosing regimen. Blinding was maintained by administration of a montelukast-matching placebo capsule every evening (PM). Albuterol aerosol was provided as a rescue inhalation.

Reporting group title	FP + GSK2190915 100 mg

Reporting group description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. GSK2190915 100 mg AM was added to the dosing regimen. Blinding was maintained by PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Reporting group title	FP + GSK2190915 300 mg

Reporting group description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. GSK2190915 300 mg AM was added to the dosing regimen. Blinding was maintained by PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Reporting group title	FP + Montelukast

Reporting group description:

Participants received FP 100 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Montelukast 10 mg capsule administered PM was added to the dosing regimen. Blinding was maintained by AM administration of GSK2190915-matching placebo tablets. Albuterol aerosol was provided as a rescue inhalation.

Reporting group title	FP / Salmeterol

Reporting group description:

Participants received a combination of FP 100 µg and salmeterol 50 µg oral inhalation BID for 6 weeks (first 3 weeks considered as active washout), in one of the 4 treatment periods. Montelukast 10 mg capsule administered PM was added to the dosing regimen. Blinding was maintained by AM administration of GSK2190915-matching placebo tablets and PM administration of a montelukast-matching placebo capsule. Albuterol aerosol was provided as a rescue inhalation.

Serious adverse events	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 104 (0.00%)	1 / 103 (0.97%)	0 / 96 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 104 (0.00%)	1 / 103 (0.97%)	0 / 96 (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

Serious adverse events	FP + Montelukast	FP / Salmeterol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 99 (0.00%)	0 / 104 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 99 (0.00%)	0 / 104 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	FP + Placebo	FP + GSK2190915 100 mg	FP + GSK2190915 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 104 (7.69%)	3 / 103 (2.91%)	4 / 96 (4.17%)
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	6 / 104 (5.77%)	1 / 103 (0.97%)	1 / 96 (1.04%)
occurrences (all)	6	1	1
Sinusitis			
subjects affected / exposed	2 / 104 (1.92%)	2 / 103 (1.94%)	3 / 96 (3.13%)
occurrences (all)	2	2	3

Non-serious adverse events	FP + Montelukast	FP / Salmeterol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 99 (1.01%)	1 / 104 (0.96%)	
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			

subjects affected / exposed	1 / 99 (1.01%)	1 / 104 (0.96%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 104 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2010	To change the Medical Monitor, To provide rationale for only including females in the study, To change Inclusion Criterion to allow only female subjects to be enrolled into the study, To amend Inclusion Criterion so that the restriction on the FEV1/FVC ratio >0.70 applied to current and former subjects only, To remove the reference to oral (for example, bambuterol) or inhaled (for example, salmeterol/formoterol) long acting beta2-agonists being stopped on the morning prior to Visit 1 as these were already prohibited 2 weeks prior to Visit 1, To remove the adjustment for gender in the analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported