



Clinical trial results:

A randomized, double-blind, double-dummy, parallel group study evaluating the safety of fluticasone propionate/salmeterol 100/50mcg HFA (2 inhalations of 50/25mcg) twice daily compared with fluticasone propionate 100mcg HFA (2 inhalations of 50mcg) twice daily in subjects 4-11 years of age with persistent asthma.

Summary

EudraCT number	2006-001417-16
Trial protocol	DE LT LV ES
Global end of trial date	28 January 2008

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	05 June 2015

Trial information

Trial identification

Sponsor protocol code	SFA106484
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00441441
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 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,

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	28 January 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety of fluticasone propionate/salmeterol 100/50mcg HFA twice daily compared with fluticasone propionate 100mcg HFA twice daily in subjects 4-11 years of age with persistent asthma

Protection of trial subjects:

The study procedures were not expected to present any pain, distress or discomfort to study participants. The therapeutic intervention were Fluticasone propionate/salmeterol HFA (50/25mcg per actuation (ex-valve) 45/21mcg per actuation (ex-actuator)) or Fluticasone propionate HFA (50mcg per actuation (exvalve) 44mcg per actuation (exactuator)). Information pertaining to study procedures was disclosed in the informed consent form presented to each prospective study subject, required reviewed and subject's signature, prior to study participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Chile: 54
Country: Number of subjects enrolled	Costa Rica: 24
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Latvia: 2
Country: Number of subjects enrolled	Lithuania: 13
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Peru: 27
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 98
Worldwide total number of subjects	351
EEA total number of subjects	69

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)	351
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 351 participants were enrolled in the study. However, only 350 of these 351 participants comprised the Intent-to-Treat Population, defined as all participants who were randomly assigned to treatment and received ≥ 1 dose of Double-Blind study treatment.

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	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)

Arm description:

Participants who were randomly assigned to Fluticasone Propionate/salmeterol 100/50 micrograms (μg) HFA (2 inhalations of 50/25 μg), twice daily for 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fluticasone propionate/salmeterol HFA (50/25mcg per actuation (ex-valve) 45/21mcg per actuation (ex-actuator))
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

Fluticasone propionate/salmeterol HFA (50/25mcg per actuation (ex-valve) 45/21mcg per actuation (ex-actuator)) - Metered Dose Inhaler

Arm title	Fluticasone Propionate Hydrofluoroalkane (HFA)
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Arm description:

Participants who were randomly assigned to Fluticasone Propionate 100 μg HFA (2 inhalations of 50 μg), twice daily for 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fluticasone propionate HFA (50mcg per actuation (ex-valve) 44mcg per actuation (ex-actuator))
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

Fluticasone propionate HFA (50mcg per actuation (ex-valve) 44mcg per actuation (ex-actuator)) - Metered Dose Inhaler

Number of subjects in period 1^[1]	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)
Started	173	177
Completed	162	163
Not completed	11	14
Consent withdrawn by subject	1	2
Adverse event, non-fatal	2	1
Not specified	3	3
Exacerbation of asthma	1	2
Protocol deviation	4	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 351 participants were enrolled in the study. However, only 350 of these 351 participants were randomized to receive treatment.

Baseline characteristics

Reporting groups

Reporting group title	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)
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Reporting group description:

Participants who were randomly assigned to Fluticasone Propionate/salmeterol 100/50 micrograms (µg) HFA (2 inhalations of 50/25 µg), twice daily for 12 weeks.

Reporting group title	Fluticasone Propionate Hydrofluoroalkane (HFA)
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Reporting group description:

Participants who were randomly assigned to Fluticasone Propionate 100 µg HFA (2 inhalations of 50 µg), twice daily for 12 weeks.

Reporting group values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)	Total
Number of subjects	173	177	350
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	7.7 ± 2.1	7.6 ± 2.12	-
Gender categorical Units: Subjects			
Female	66	71	137
Male	107	106	213
Race, Customized Units: Subjects			
White/Caucasian/European Heritage	114	113	227
American Indian or Alaska Native	24	27	51
Central/South Asian Heritage	8	8	16
African American/African Heritage	7	8	15
Japanese Heritage	3	0	3
Arabic/North African Heritage	2	2	4
South East Asian Heritage	2	0	2
Mixed Race	13	19	32
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	70	73	143
Not Hispanic or Latino	103	104	207

End points

End points reporting groups

Reporting group title	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)
Reporting group description: Participants who were randomly assigned to Fluticasone Propionate/salmeterol 100/50 micrograms (µg) HFA (2 inhalations of 50/25 µg), twice daily for 12 weeks.	
Reporting group title	Fluticasone Propionate Hydrofluoroalkane (HFA)
Reporting group description: Participants who were randomly assigned to Fluticasone Propionate 100 µg HFA (2 inhalations of 50 µg), twice daily for 12 weeks.	
Subject analysis set title	Fluticasone Propionate/Salmeterol HFA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomly assigned to Fluticasone Propionate/salmeterol 100/50 micrograms (µg) HFA (2 inhalations of 50/25 µg), twice daily for 12 weeks. The Cortisol Population included all participants not excluded due to the following reasons: missing data, use of protocol-specified corticosteroids (prior to screening), collection time outside of 24 ± 2 hours, use of inhaled cortical steroid (ICS) during treatment, and who stopped study medication >1 day prior to start of postbaseline urine collection.	
Subject analysis set title	Fluticasone Propionate HFA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who were randomly assigned to Fluticasone Propionate 100 µg HFA (2 inhalations of 50 µg), twice daily for 12 weeks. The Cortisol Population included all participants not excluded due to the following reasons: missing data, use of protocol-specified corticosteroids (prior to screening), collection time outside of 24 ± 2 hours, use of inhaled cortical steroid (ICS) during treatment, and who stopped study medication >1 day prior to start of postbaseline urine collection.	
Subject analysis set title	Fluticasone Propionate/Salmeterol HFA - Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluticasone propionate/salmeterol 100/50 micrograms (µg) HFA (2 inhalations of 50/25µg) twice daily in participants 4-11 years of age for 12 weeks - Participants who also used Spacers	
Subject analysis set title	Fluticasone Propionate/Salmeterol HFA - No Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluticasone propionate/salmeterol 100/50 µg HFA (2 inhalations of 50/25 µg) twice daily in participants 4-11 years of age for 12 weeks	
Subject analysis set title	Fluticasone Propionate HFA - Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluticasone Propionate 100 µg HFA (2 inhalation of 50 µg) twice daily in participants 4-11 years of age for 12 weeks. Participants who also used Spacers	
Subject analysis set title	Fluticasone Propionate HFA - No Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Fluticasone Propionate 100 µg HFA (2 inhalation of 50 µg) twice daily in participants 4-11 years of age for 12 weeks	

Subject analysis set title	FP/S HFA or FP HFA - No Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who did not use spacer and were in either treatment group of Fluticasone propionate/salmeterol 100/50 µg (FP/S) HFA (2 inhalations of 50/25 µg) or Fluticasone Propionate 100 µg (FP) HFA (2 inhalations of 50 µg) twice daily in participants 4-11 years of age for 12 weeks	
Subject analysis set title	FP/S HFA or FP HFA - Spacer
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who required a spacer and were in either treatment group of Fluticasone propionate/salmeterol 100/50 micrograms (µg) (FP/S) HFA (2 inhalations of 50/25 µg) or Fluticasone Propionate 100 µg (FP) HFA (2 inhalations of 50 µg) twice daily in participants 4-11 years of age for 12 weeks.	

Primary: Possible Drug-Related Adverse Events

End point title	Possible Drug-Related Adverse Events ^[1]
End point description:	
Adverse Events reported by the Investigator and judged by the Investigator to be possibly related to study drug, categorized by the Medical Dictionary for Regulatory Activities (MedRA), were reported. ECG, electrocardiogram. QTc (corrected QT interval) and QT represent intervals on an ECG. The Intent-to-Treat (ITT) Population was used which includes all participants who were randomized and received at least one dose of double-blind study treatment.	
End point type	Primary
End point timeframe:	
Treatment period (weeks 1-12) and Post Treatment (≥1 day after last time study drug)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	177		
Units: Participants				
number (not applicable)				
Participants with any drug-related event	13	16		
Investigations - ECG QTc interval prolonged	9	4		
Investigations - QT interval prolonged	0	2		
Investigations - ECG QT borderline prolonged	1	0		
Investigations - ECG QT interval abnormal	1	0		
Cardiac - Defect conduction intraventricular	2	7		
Cardiac - Conduction disorder	1	1		
Cardiac - Sinus tachycardia	1	0		
Cardiac - Supraventricular ectopics	0	1		
Infections/Infestations - Oral candidiasis	0	1		
Infections/Infest - Oropharyngeal candidiasis	0	1		

Respiratory/thoracic/mediastinal - Dysphonia	2	0		
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Statistical analyses

No statistical analyses for this end point

Primary: Investigator Evaluations of Electrocardiogram (ECG) Results

End point title	Investigator Evaluations of Electrocardiogram (ECG) Results ^[2]
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End point description:

ECGs were transmitted to an independent cardiologist who was responsible for providing interpretation of the ECG as either normal or abnormal (based on personal assessment). The investigator was then responsible for determining the clinical significance of the abnormal ECG in the context of the participants' history and clinical presentation. An abnormal, clinically significant ECG included, but was not limited to: prolonged QT interval, ischemic changes, ventricular hypertrophy, intraventricular conduction abnormalities, and clinically significant arrhythmias. PD, premature discontinuation. The number of participants at baseline was 173 and 177, respectively, for the Fluticasone propionate/salmeterol HFA and Fluticasone Propionate (FP) HFA groups. The number of participants at Week 12 was 162 and 160, respectively. Data for 6 participants in the FP treatment arm were either not obtained or not evaluable.

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[3]	177 ^[4]		
Units: participants				
number (not applicable)				
Baseline - Normal	145	155		
Baseline - Abnormal: Not Clinically Significant	27	21		
Baseline - Abnormal: Clinically Significant	1	0		
Week 12-No Change or insignificant Change	136	142		
Week 12-Clinically Significant Change-Favorable	2	0		
Week 12-Clinically Significant Change-Unfavorable	24	18		
PD-No Change or insignificant Change	7	9		

PD-Clinically Significant Change-Favorable	0	1		
PD-Clinically Significant Change-Unfavorable	0	1		

Notes:

[3] - ITT Population

[4] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Unfavorable ECGs at Week 12

End point title	Clinically Significant Unfavorable ECGs at Week 12 ^[5]
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End point description:

Post-randomization ECGs categorized by the primary investigator as no change, significant change (favorable), significant change (unfavorable) from the ECG performed at Visit 1 (Baseline) are presented. Significant change (favorable) includes any ECG that improved from baseline, whereas significant change (unfavorable) includes any ECG that worsened from baseline. Clinical significance is determined by the primary investigator. The number of participants at baseline was 173 and 177, respectively, for the Fluticasone propionate/salmeterol HFA and Fluticasone Propionate (FP) HFA groups. The numbers of participants at Week 12 were 162 and 160, respectively. Data for 6 participants in the FP treatment arm were either not obtained or not evaluable.

End point type	Primary
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End point timeframe:

Baseline, Week 12

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[6]	177 ^[7]		
Units: participants				
number (not applicable)				
Clinically significant unfavorable change	24	18		
AEs Reported for ECG findings	22	18		
Clinically significant unfavorable ECGs repeated	11	11		
Repeated ECGs w/ no change or insignificant change	6	5		

Notes:

[6] - ITT Population

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: ECG Measures - Heart Rate

End point title	ECG Measures - Heart Rate ^[8]
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End point description:

The range of heart rates for this study was between 49-144 beats per minute

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[9]	177 ^[10]		
Units: beats per minute				
arithmetic mean (full range (min-max))				
Mean Heart Rate - Baseline	84 (53 to 144)	82.6 (51 to 136)		
Mean Heart Rate - Week 12	85.5 (59 to 138)	81.9 (52 to 121)		
Mean Heart Rate - Premature Discontinuation	73.1 (53 to 90)	92.4 (49 to 130)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: ECG Measures - QT Interval

End point title	ECG Measures - QT Interval ^[11]
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End point description:

Fridericia's formula $QT_c \text{ interval} = QT \text{ interval} / \text{cubed root of the R-R interval}$. The Bazett's formula $QT_c = QT / \text{squared root of the R-R interval}$.

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[12]	177 ^[13]		
Units: milliseconds				
arithmetic mean (full range (min-max))				
Mean QTc Interval (Fridericia)- Baseline	394.5 (340 to 449)	390.8 (338 to 429)		
Mean QTc Interval (Fridericia) - Week 12	397.5 (355 to 439)	393.6 (329 to 449)		
Premature Discontinuation (Fridericia)	392 (359 to 417)	394.8 (376 to 408)		
Mean QTc Interval (Bazett) - Baseline	416.3 (356 to 464)	411.4 (346 to 471)		
Mean QTc Interval (Bazett) - Week 12	420.8 (368 to 466)	413.7 (351 to 477)		
Premature Discontinuation (Bazett)	403.3 (376 to 446)	422.7 (378 to 454)		

Notes:

[12] - ITT Population

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Cardiovascular Adverse Events Reported During Treatment Period

End point title	Cardiovascular Adverse Events Reported During Treatment Period ^[14]
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End point description:

Cardiovascular Adverse Events, as categorized by the Medical Dictionary for Regulatory Activities (MedDRA), reported during Treatment Period. The Adverse Events were identified in any ECG interpretation by a central reader (Cardiologist) for any ECG obtained after the first treatment dose and were then reported by the Primary Investigator as an Adverse Event. Please see the category titles for a list of candidate cardiovascular adverse events.

End point type	Primary
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End point timeframe:

12-Week Treatment Period

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[15]	177 ^[16]		
Units: participants				
number (not applicable)				
Participants with Any Event	98	103		

Electrocardiogram (ECG) Change	3	2		
ECG QTc Interval Prolonged	2	1		
ECG Abnormal	1	1		
ECG QT Borderline Prolonged	1	0		
Defect Conduction Intraventricular	4	3		
Cardiac Arrhythmia	1	0		
Premature Atrial Contraction	1	0		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Cardiovascular Adverse Events Reported During the Post-Treatment Period

End point title	Cardiovascular Adverse Events Reported During the Post-Treatment Period ^[17]
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End point description:

Cardiovascular Adverse Events, as categorized by the Medical Dictionary for Regulatory Activities (MedDRA), reported during Post-treatment period, defined as 1 day after last dose of study drug. The Adverse Events were identified in any ECG interpretation by a central reader (Cardiologist) for any ECG obtained after the first treatment dose and were then reported by the Primary Investigator as an Adverse Event.

End point type	Primary
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End point timeframe:

5 Days after Week 12

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[18]	177 ^[19]		
Units: participants				
number (not applicable)				
Participants with Any Event	19	19		
ECG QTc interval prolonged	11	5		
QT interval prolonged	1	2		
ECG QT interval Abnormal	1	0		
Defect Conduction Intraventricular	2	7		
Conduction disorder	1	1		
Sinus Tachycardia	1	0		
Supraventricular Ectopics	0	1		

Notes:

[18] - ITT Population

[19] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Asthma Exacerbations: Worsening of Asthma Requiring Emergency Intervention, Hospitalization, or Treatment With Asthma Medications Prohibited by the Protocols

End point title	Asthma Exacerbations: Worsening of Asthma Requiring Emergency Intervention, Hospitalization, or Treatment With Asthma Medications Prohibited by the Protocols ^[20]
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End point description:

The Primary Investigator determined the severity of the exacerbation based on the participant's clinical presentation and the investigator's understanding of the disease, the participant, and his or her clinical experiences. The severity of the exacerbation was not defined in the protocol. Mild: Usually treated at home. Prompt relief with inhaled short-acting beta2 agonist. Possible short course of oral systemic corticosteroids. Moderate: Usually requires office or emergency department visit. Relief with frequent inhaled short-acting beta2 agonist. Oral systemic corticosteroids; some symptoms last for 1-2 days after treatment begins. Severe: Usually requires emergency department visit and likely hospitalization. Partial relief with frequent inhaled short-acting beta2 agonist. Oral systemic corticosteroids; some symptoms last for more than 3 days after treatment begins. Adjunctive therapies are helpful.

End point type	Primary
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End point timeframe:

Treatment period (weeks 1-12)

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[21]	177 ^[22]		
Units: participants				
number (not applicable)				
Participants with any asthma exacerbation	1	3		
Severity - Mild	1	2		
Severity - Moderate/Severe	0	1		
Withdrawal due to Asthma Exacerbation	1	2		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With the Indicated Levels of 24-hour Urinary Cortisol Excretion

End point title	Number of Participants With the Indicated Levels of 24-hour
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End point description:

"Abnormal high cortisol excretion" and "Abnormal low cortisol excretion" are defined as above the upper limit of normal and below the lower limit of normal, respectively. The normal range for cortisol levels vary by age and gender. An abnormality is defined as a value of 24-hour urinary cortisol excretion that is outside the normal range. The normal range for 24-hour urinary cortisol excretion was provided by the central laboratory. The Cortisol Population was used which included all participants not excluded due to the following reasons: missing data, use of protocol-specified corticosteroids (prior to screening), collection time outside of 24 ± 2 hours, use of inhaled corticosteroid (ICS) during treatment, and who stopped study medication >1 day prior to start of postbaseline urine collection.

End point type	Primary
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End point timeframe:

Baseline and week 12

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA	Fluticasone Propionate HFA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	147 ^[24]	144 ^[25]		
Units: participants				
number (not applicable)				
Baseline - Abnormal high cortisol excretion, n	13	17		
Baseline - Abnormal low cortisol excretion, n	1	0		
Week 12 - Abnormal high cortisol excretion, n	13	8		
Week 12 - Abnormal low cortisol excretion, n	2	0		

Notes:

[24] - Cortisol Population

[25] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Values of 24-hour Urinary Cortisol Excretion at Baseline and Week 12

End point title	Geometric Mean Values of 24-hour Urinary Cortisol Excretion at Baseline and Week 12 ^[26]
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End point description:

Normal range for Cortisol levels vary by age and gender. Geometric mean is the product of the values taken to the Nth root, where N is the number of values in the set of values.

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA	Fluticasone Propionate HFA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	147 ^[27]	144 ^[28]		
Units: Nanomoles per 24 hours (nmol/24 hrs)				
geometric mean (full range (min-max))				
Baseline - Geometric Mean	32.71 (2.7 to 156.2)	30.88 (4.2 to 891.6)		
Week 12 - Geometric Mean	25.03 (1.7 to 152.6)	23.17 (5.3 to 145.8)		

Notes:

[27] - Cortisol Population

[28] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Ratio for Week12:Baseline for 24-hour Urinary Cortisol Excretion

End point title	Geometric Mean Ratio for Week12:Baseline for 24-hour Urinary Cortisol Excretion ^[29]
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End point description:

Normal range for Cortisol levels vary by age and gender. The data provided are a direct calculation of the Week 12

geometric mean divided by the baseline value, nanomoles per 24 hours (nmol/24 hrs).

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA	Fluticasone Propionate HFA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	147 ^[30]	144 ^[31]		
Units: ratio				
number (not applicable)	0.77	0.75		

Notes:

[30] - Cortisol Population

[31] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With the Indicated Levels of 24 Hour Urinary Cortisol Excretion by Spacer Use

End point title	Number of Participants With the Indicated Levels of 24 Hour Urinary Cortisol Excretion by Spacer Use ^[32]
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End point description:

AeroChamber Plus spacers were provided for participants who demonstrated the inability to coordinate the use of an Meter Dose Inhaler at Visit 1. AeroChamber Plus spacer delivers 22% more medication than the original AeroChamber and is available in three mask sizes and without a mask. "Abnormal high cortisol excretion" and "Abnormal low cortisol excretion" are defined as above the upper limit of normal and below the lower limit of normal, respectively. An abnormality is defined as a value of 24-hour urinary cortisol excretion that is outside the normal range. The normal range for 24-hour urinary cortisol excretion was provided by the central laboratory.

End point type	Primary
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End point timeframe:

Baseline and Week 12

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA - Spacer	Fluticasone Propionate/Salmeterol HFA - No Spacer	Fluticasone Propionate HFA - Spacer	Fluticasone Propionate HFA - No Spacer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	115 ^[33]	32 ^[34]	113 ^[35]	31 ^[36]
Units: participants				
number (not applicable)				
Baseline - Abnormal high cortisol excretion	12	1	14	3
Baseline - Abnormal low cortisol excretion	0	1	0	0
Week 12 - Abnormal high cortisol excretion	10	3	7	1
Week 12 - Abnormal low cortisol excretion	2	0	0	0

Notes:

[33] - Cortisol Population

[34] - Cortisol Population

[35] - Cortisol Population

[36] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Values of 24 Hour Urinary Cortisol Excretion by Spacer Use at Baseline and Week 12

End point title	Geometric Mean Values of 24 Hour Urinary Cortisol Excretion by Spacer Use at Baseline and Week 12 ^[37]
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End point description:

AeroChamber Plus spacers were provided for participants who demonstrated the inability to coordinate the use of an Meter Dose Inhaler at Visit 1. AeroChamber Plus spacer delivers 22% more medication than the original AeroChamber

and is available in three mask sizes and without a mask. Geometric mean is the product of the values taken to the Nth root, where N is the number of values in the set of values.

End point type	Primary
End point timeframe:	
Baseline and Week 12	

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA - Spacer	Fluticasone Propionate/Salmeterol HFA - No Spacer	Fluticasone Propionate HFA - Spacer	Fluticasone Propionate HFA - No Spacer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	115 ^[38]	32 ^[39]	113 ^[40]	31 ^[41]
Units: Nanomoles per 24 hours (nmol/24 hrs)				
geometric mean (full range (min-max))				
Baseline - Geometric Mean	31.89 (3.6 to 156.2)	35.84 (2.7 to 143.3)	30.61 (4.2 to 891.6)	31.89 (7.9 to 335)
Week 12 - Geometric Mean	23.37 (1.7 to 143.3)	32.05 (4.6 to 152.6)	23.2 (5.3 to 103.2)	23.06 (5.4 to 145.8)

Notes:

[38] - Cortisol Population

[39] - Cortisol Population

[40] - Cortisol Population

[41] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Ratio for Week12: Baseline for 24 Hour Urinary Cortisol Excretion by Spacer Use

End point title	Geometric Mean Ratio for Week12: Baseline for 24 Hour Urinary Cortisol Excretion by Spacer Use ^[42]
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End point description:

AeroChamber Plus spacers were provided for participants who demonstrated the inability to coordinate the use of an Meter Dose Inhaler at Visit 1. AeroChamber Plus spacer delivers 22% more medication than the original AeroChamber and is available in three mask sizes and without a mask. The data provided are a direct calculation of the Week 12 geometric mean divided by the baseline value, nanomoles per 24 hours (nmol/24 hrs).

End point type	Primary
End point timeframe:	
Baseline and Week 12	

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analysis for this endpoint.

End point values	Fluticasone Propionate/Salmeterol HFA - Spacer	Fluticasone Propionate/Salmeterol HFA - No Spacer	Fluticasone Propionate HFA - Spacer	Fluticasone Propionate HFA - No Spacer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	115 ^[43]	32 ^[44]	113 ^[45]	31 ^[46]
Units: ratio				
number (not applicable)	0.73	0.89	0.76	0.72

Notes:

[43] - Cortisol Population

[44] - Cortisol Population

[45] - Cortisol Population

[46] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinic Morning (AM) Forced Expiratory Volume in Participants 6-11 Years

End point title	Clinic Morning (AM) Forced Expiratory Volume in Participants 6-11 Years
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End point description:

FEV1 (Forced Expiratory Volume in 1 second) is the volume of air that can be forced out in one second, after taking a deep breath. FEV1 is measured using a spirometer and obtaining "best effort" from 3 to 8 measurements. Week 12 is the measure taken at Week 12. A Subset of the ITT Population included participants who were 6-11 years of age (population not necessarily selected to show efficacy differences). Total numbers of participants analyzed for the Fluticasone propionate (FP)/salmeterol HFA and FP groups, respectively, were 137 and 136 at baseline; 126 and 124 at Week 12, and 6 and 7 at premature discontinuation.

End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137 ^[47]	136 ^[48]		
Units: Liters per second (L/sec)				
arithmetic mean (standard error)				
Baseline - Mean FEV1	1.67 (± 0.035)	1.64 (± 0.035)		
Week 12 - Mean FEV1	1.91 (± 0.038)	1.82 (± 0.036)		
Week 12 - Mean Change from baseline	0.24 (± 0.023)	0.18 (± 0.023)		
Premature discontinuation - Mean FEV1	1.81 (± 0.14)	1.7 (± 0.212)		
Premature discontin. - Mean Change from baseline	0.03 (± 0.09)	-0.07 (± 0.12)		

Notes:

[47] - Subset of ITT Population

[48] - Subset of ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: AM Peak Expiratory Flow

End point title	AM Peak Expiratory Flow
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End point description:

The peak expiratory flow (PEF) rate measures how fast a person can exhale air. It is used to compare to normal flow

rates to predict obstruction and disease. The average PEF for a child or adolescent whose height is 43 inches is

147 Liters/minute (L/min), whose height is 66 inches is 454 L/min. Triplicate measurements taken for the best effort

recorded. Participants from the ITT Population (not necessarily selected to show efficacy differences) were analyzed. Total numbers of participants analyzed for the Fluticasone

propionate (FP)/salmeterol HFA and FP groups, respectively, were 173 and 175 at baseline; 173 and 174 at Weeks 1-12; and 171 and 173 for the last 7 days on treatment.

End point type	Secondary
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End point timeframe:

Baseline and 12-Week Treatment Period

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[49]	177 ^[50]		
Units: Liters/minute (L/min)				
arithmetic mean (standard error)				
Baseline - Mean AM PEF	213 (± 4.83)	203 (± 4.37)		
Weeks 1-12 - Mean AM PEF	233 (± 5.07)	220 (± 4.43)		
Weeks 1-12 - Mean Change from Baseline	20.2 (± 2.04)	17.4 (± 1.86)		
Last 7 Days on Treatment - Mean AM PEF	238 (± 5.39)	226 (± 4.73)		
Last 7 Days on Treatment-Mean Change from Baseline	25.3 (± 2.58)	23.3 (± 2.47)		

Notes:

[49] - ITT Population

[50] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Symptom Scores

End point title	Asthma Symptom Scores
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End point description:

Each morning prior dosing or PEF, self-scored based on past 24 hours: 0=No symptoms, 1=Symptoms for one short

period, 2=Symptoms for two or more short periods, 3=Frequent Symptoms which did not affect activities of daily living

(ADL), 4=Frequent. Participants from the ITT population (not necessarily selected to show efficacy

differences) were analyzed. Total numbers of participants analyzed for the Fluticasone propionate (FP)/salmeterol HFA and FP groups, respectively, were 173 and 175 at baseline; 172 and 174 at Weeks 1-12; and 167 and 170 for the last 7 days on treatment.

End point type	Secondary
End point timeframe:	
Baseline and 12-Week Treatment Period	

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[51]	177 ^[52]		
Units: Score in scale				
arithmetic mean (standard deviation)				
Baseline - Mean Score	1.3 (± 0.06)	1.4 (± 0.06)		
Weeks 1-12 - Mean Score	0.9 (± 0.06)	0.8 (± 0.05)		
Weeks 1-12 - Mean change from baseline	-0.4 (± 0.06)	-0.6 (± 0.06)		
Last 7 Days on Treatment - Mean Score	0.8 (± 0.07)	0.8 (± 0.07)		
Last 7 Days on Treat. - Mean change from baseline	-0.5 (± 0.07)	-0.6 (± 0.08)		

Notes:

[51] - ITT population

[52] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Symptom Free Days

End point title	Percentage of Symptom Free Days
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End point description:

Percentage of number of days without asthma symptoms based on Asthma Symptom Scores. Each morning prior to dosing or PEF, asthma symptoms were self-scored based on the past 24 hours: 0=no symptoms, 1=symptoms for one short period, 2=symptoms for two or more short periods, 3=frequent symptoms that did not affect activities of daily living (ADL), 4=frequent. Participants from the ITT population (not necessarily selected to show efficacy differences) were analyzed. Total numbers of participants analyzed for the Fluticasone propionate (FP)/salmeterol HFA and FP groups, respectively, were 173 and 175 at baseline; 172 and 174 at Weeks 1-12; and 167 and 170 for the last 7 days on treatment.

End point type	Secondary
End point timeframe:	
Baseline and 12-Week Treatment Period	

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[53]	177 ^[54]		
Units: Percentage of days				
arithmetic mean (standard error)				
Baseline - Mean Percent	20 (± 2.02)	18.4 (± 2)		
Weeks 1-12 - Mean Percent	46.7 (± 2.77)	48.7 (± 2.8)		
Weeks 1-12 - Mean change from baseline	26.8 (± 2.47)	30.5 (± 2.62)		
Last 7 Days on Treatment - Mean Percent	51.9 (± 3.51)	53.4 (± 3.44)		
Last 7 Days on Treat. - Mean change from baseline	32.1 (± 3.32)	34.9 (± 3.43)		

Notes:

[53] - ITT population

[54] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Albuterol Use

End point title	Albuterol Use
End point description:	
Albuterol inhalation aerosol was used as a rescue or prophylactic and recorded daily by subject or caregiver. The number of puffs of albuterol over the previous 24 hour period prior to dosing was recorded. Participants from the ITT population (not necessarily selected to show efficacy differences) were analyzed. Total numbers of participants analyzed for the Fluticasone propionate (FP)/salmeterol HFA and FP groups, respectively, were 168 and 174 at baseline; 166 and 172 at Weeks 1-12; and 157 and 165 for the last 7 days on treatment.	
End point type	Secondary
End point timeframe:	
Baseline and 12-Week Treatment Period	

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[55]	177 ^[56]		
Units: Number of puffs per 24 hours				
arithmetic mean (standard error)				
Baseline - Mean number of puffs	1.5 (± 0.12)	1.8 (± 0.19)		
Weeks 1-12 - Mean number of puffs	1 (± 0.09)	0.9 (± 0.09)		
Weeks 1-12 - Mean change from baseline	-0.6 (± 0.12)	-1 (± 0.16)		
Last 7 Days on Treatment - Mean number of puffs	0.7 (± 0.11)	0.7 (± 0.11)		

Last 7 Days on Treat. - Mean change from baseline	-0.8 (\pm 0.15)	-1.2 (\pm 0.19)		
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Notes:

[55] - ITT population

[56] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Albuterol-free Days

End point title	Percent of Albuterol-free Days
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End point description:

Percentage of days when Albuterol use was unnecessary based on daily record and symptom free days. Participants from the ITT population (not necessarily selected to show efficacy differences) were analyzed. Total numbers of participants analyzed for the Fluticasone propionate (FP)/salmeterol HFA and FP groups, respectively, were 168 and 174 at baseline; 166 and 172 at Weeks 1-12; and 157 and 165 for the last 7 days on treatment.

End point type	Secondary
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End point timeframe:

Baseline and 12-Week Treatment Period

End point values	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 ^[57]	177 ^[58]		
Units: Percentage of days				
arithmetic mean (standard error)				
Baseline - Mean percent rescue free	43.7 (\pm 2.85)	42.5 (\pm 3.04)		
Weeks 1-12 - Mean percent rescue free	67.1 (\pm 2.46)	70 (\pm 2.4)		
Weeks 1-12 - Mean change from baseline	23.6 (\pm 2.79)	28.3 (\pm 2.93)		
Last 7 Days on Treat. - Mean percent rescue free	75.4 (\pm 2.96)	75.8 (\pm 2.98)		
Last 7 Days on Treat. - Mean change from baseline	30.4 (\pm 3.5)	32.8 (\pm 3.58)		

Notes:

[57] - ITT population

[58] - ITT population

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric Mean Values of 24-hour Urinary Cortisol Excretion at Baseline and Week 12

End point title	Geometric Mean Values of 24-hour Urinary Cortisol Excretion at Baseline and Week 12
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End point description:

A post-hoc analysis excluding participants with urine cortisol baseline values of >200 nanomoles/24 hours. Geometric mean is the product of the values taken to the Nth root, where N is the number of values in the set of values.

End point type	Post-hoc
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End point timeframe:

Baseline and Week 12

End point values	Fluticasone Propionate/Salmeterol HFA	Fluticasone Propionate HFA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	147 ^[59]	140 ^[60]		
Units: Nanamoles per 24 hours (nmol/24 hrs)				
geometric mean (full range (min-max))				
Baseline - Geometric Mean	32.71 (2.7 to 156.2)	28.39 (4.2 to 146.9)		
Week 12 - Geometric Mean	25.03 (1.7 to 152.6)	22.8 (5.3 to 145.8)		

Notes:

[59] - Cortisol Population

[60] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric Mean Ratio for Baseline:Week12 24-hour Urinary Cortisol Excretion

End point title	Geometric Mean Ratio for Baseline:Week12 24-hour Urinary Cortisol Excretion
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End point description:

A post-hoc analysis excluding participants with urine cortisol baseline values of >200 nmol/24 hrs. The data provided are a direct calculation of the Week 12 geometric mean divided by the baseline value, nanomoles per 24 hours (nmol/24 hrs).

End point type	Post-hoc
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End point timeframe:

Baseline and Week 12

End point values	Fluticasone Propionate/Salmeterol HFA	Fluticasone Propionate HFA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	147 ^[61]	140 ^[62]		
Units: ratio				
number (not applicable)	0.77	0.8		

Notes:

[61] - Cortisol Population

[62] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric Mean Values of 24-hour Urinary Cortisol Excretion by Spacer Use Excluding Participants With Abnormal Urinary Cortisol Excretion Values at Baseline From the Cortisol Population at Baseline and Week 12

End point title	Geometric Mean Values of 24-hour Urinary Cortisol Excretion by Spacer Use Excluding Participants With Abnormal Urinary Cortisol Excretion Values at Baseline From the Cortisol Population at Baseline and Week 12
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End point description:

AeroChamber Plus spacers were provided for participants who demonstrated the inability to coordinate the use of an Meter Dose Inhaler at Visit 1. AeroChamber Plus spacer delivers 22% more medication than the original AeroChamber and is available in three mask sizes and without a mask. Geometric mean is the product of the values taken to the Nth root, where N is the number of values in the set of values.

End point type	Post-hoc
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End point timeframe:

Baseline and Week 12

End point values	FP/S HFA or FP HFA - No Spacer	FP/S HFA or FP HFA - Spacer		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58 ^[63]	202 ^[64]		
Units: Nanomoles per 24 hr (nmoles/24 hr)				
geometric mean (full range (min-max))				
Baseline - Geometric Mean	31.88 (7.9 to 81.7)	27.08 (3.6 to 166.3)		
Week 12 - Geometric Mean	27.85 (5.4 to 152.6)	22.38 (1.7 to 143.3)		

Notes:

[63] - Cortisol Population

[64] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Post-hoc: Geometric mean ratio for Baseline:Week 12 24-hour Urinary Cortisol Excretion by Spacer use Excluding Participants with Abnormal Urinary Cortisol Excretion Values at Baseline from the Cortisol Population

End point title	Geometric mean ratio for Baseline:Week 12 24-hour Urinary Cortisol Excretion by Spacer use Excluding Participants with
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End point description:

AeroChamber Plus spacers were provided for participants who demonstrated the inability to coordinate the use of an Meter Dose Inhaler at Visit 1. AeroChamber Plus spacer delivers 22% more medication than the original AeroChamber and is available in three mask sizes and without a mask. The data provided are a direct calculation of the Week 12 geometric mean divided by the baseline value, nanomoles per 24 hours (nmol/24 hrs).

End point type Post-hoc

End point timeframe:

Baseline and Week 12

End point values	FP/S HFA or FP HFA - No Spacer	FP/S HFA or FP HFA - Spacer		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58 ^[65]	202 ^[66]		
Units: ratio				
number (not applicable)	0.87	0.83		

Notes:

[65] - Cortisol Population

[66] - Cortisol Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment period (weeks 1-12) and Post Treatment (≥ 1 day after last time study drug)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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Reporting groups

Reporting group title	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)
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Reporting group description:

Participants who were randomly assigned to Fluticasone Propionate/salmeterol 100/50 micrograms (μg) HFA (2 inhalations of 50/25 μg), twice daily for 12 weeks.

Reporting group title	Fluticasone Propionate Hydrofluoroalkane (HFA)
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Reporting group description:

Participants who were randomly assigned to Fluticasone Propionate 100 μg HFA (2 inhalations of 50 μg), twice daily for 12 weeks.

Serious adverse events	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 173 (0.58%)	0 / 177 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head Injury due to fall			
subjects affected / exposed	1 / 173 (0.58%)	0 / 177 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Fluticasone Propionate/Salmeterol Hydrofluoroalkane (HFA)	Fluticasone Propionate Hydrofluoroalkane (HFA)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 173 (35.26%)	68 / 177 (38.42%)	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	26 / 173 (15.03%) 54	25 / 177 (14.12%) 34	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	8 / 173 (4.62%) 9	16 / 177 (9.04%) 17	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	9 / 173 (5.20%) 14	7 / 177 (3.95%) 9	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	16 / 173 (9.25%) 21 4 / 173 (2.31%) 5 8 / 173 (4.62%) 9 11 / 173 (6.36%) 11	21 / 177 (11.86%) 42 12 / 177 (6.78%) 14 6 / 177 (3.39%) 10 13 / 177 (7.34%) 13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2006	<p>Amendment 01: The protocol was amended to change the study design from a double-blind to a double-blind, double-dummy.</p> <p>The protocol was revised to clarify the following: the fluticasone propionate/salmeterol and fluticasone strengths are in ex-valve strength, to further explain the rationale of the study is to provide information on the relative safety of adding a beta2-agonist to ICS treatment, the data will be stratified by age as well as spacer use, laboratory results for subjects who rescreen taken do not need to be taken again prior to randomization, PI oversight for safety measures obtained during the study, how Reversibility is to be obtained, that one spacer should be used for both study drug inhalers and rescue medication, the Time & Events (T&E) Visit 1 is 14+or =2 days prior to Visit 2, also in the T&E table that PGx samples can be obtained at the Premature Discontinuation Visit, and finally that a throat culture should be taken in subjects with evidence of candidiasis.</p> <p>The following items were added to the protocol: a statement to Exclusion Criteria # 12 to reflect that QTc intervals > 449 will disqualify a subject from participating in the study, 24 hour Urine Collection to be done within 7 days prior to Visit 2, Historical Reversibility obtained as FEV1 or PEF is acceptable.</p> <p>The following updates were made for administrative purposes: Added UK GSK address, changed Medical Monitor Name and contact information, updated Investigator Protocol Agreement Page.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported