ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/13/2014

ClinicalTrials.gov ID: NCT00517634

Study Identification

Unique Protocol ID:	HZA109912
Brief Title:	Study Of Fluticasone Propionate/Salmeterol In Asthmatic Subjects
Official Title:	A 12-week, Randomised, Double-blind, Placebo-controlled, Three-period, Cross-over Pilot Study Comparing the Effect of Salmeterol/Fluticasone Propionate, Fluticasone Propionate and Placebo on Perpheral Blood Eosinophils and Serum IL-5 in Response to Allergen Challenge in Asthma Subjects When Allergen Challenge is Administered at 1 Hour or 11-12 Hours Post-dose of the Dosing Interval
Secondary IDs:	

Study Status

Record Verification:	March 2014
Overall Status:	Completed
Study Start:	August 2007
Primary Completion:	July 2008 [Actual]
Study Completion:	July 2008 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 50,703 Serial Number: TBD Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 07/H1003/128 Board Name: South Manchester Research Ethics Committee Board Affiliation: South Manchester Research Ethics Committee Phone: 0161-237-2268 Email: cynthia.carter@northwest.nhs.uk
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	The aim of the present study is to investigate whether the effects of salmeterol in combination with fluticasone propionate on blood markers of airway inflammation are maintained after chronic dosing and whether the effect is influenced by the time of allergen challenge relative to the time of dosing.
Detailed Description:	A 12-week, randomised, double-blind, placebo-controlled, three-period, cross-over pilot study comparing the effect of salmeterol/ fluticasone propionate, fluticasone propionate and placebo on perpheral blood eosinophils and serum IL-5 in response to allergen challenge in asthma subjects when allergen challenge is administered at 1 hour or 11-12 hours post-dose of the dosing interval

Conditions

Conditions:	Asthma
Keywords:	asthma allergen challenge IL-5 eosinophils

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	6
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Efficacy Study
Enrollment:	23 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Sequence 1: FP, SFC, Placebo Fluticasone Propionate (FP) 100 micrograms (mcg) twice daily (BID) in the first treatment period: Salmeterol/Fluticasone Propionate Combination (SFC) 50/100 mcg BID in the second treatment period: Placebo in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo
Experimental: Sequence 2: Placebo, SFC, FP Placebo in the first treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the second treatment period: Fluticasone Propionate 100 mcg BID in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo
Experimental: Sequence 3: SFC, FP, Placebo Salmeterol/Fluticasone Propionate 50/100 Combination mcg BID in the first treatment period: Fluticasone Propionate 100 mcg BID in the second treatment period: Placebo in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo
Experimental: Sequence 4: SFC, Placebo, FP Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the first treatment period: Placebo in the second treatment period: Fluticasone Propionate 100 mcg BID in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo

Arms	Assigned Interventions
Experimental: Sequence 5: FP, Placebo, SFC Fluticasone Propionate 100 mcg BID in the first treatment period: Placebo in the second treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo
Experimental: Sequence 6: Placebo, FP, SFC Placebo in the first treatment period: Fluticasone Propionate 100 mcg BID in the second treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the third treatment period	Drug: FP Fluticasone Propionate 100 mcg BD Drug: SFC Salmeterol/Fluticasone Propionate Combination 50/100 mcg BD Drug: Placebo Matching Placebo

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 55 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Informed consent.
- Outpatient.
- Male or non-pregnant/non-lactating female.
- Aged 18-55.
- Diagnosis of asthma.
- Pre-bronchodilatory FEV1 > 75% predicted.
- Using inhaled short-acting beta-2-agonists (SABA) with no inhaled corticosteroids.
- Judged capable of withholding SABA for at least 6 hours prior to visits.
- Reversibility of >12% and 200mL or PC20 of <8mg/mL.
- Demonstration of atopy

Exclusion Criteria:

- History of life-threatening asthma.
- Use of proscribed asthma medications.
- Use of anti-histamines or potent inhibitors of CYP3A4.
- Respiratory tract infection.

- Asthma exacerbation with 4 weeks of Visit 1.
- Subjects with exercise induced asthma only.
- Concurrent respiratory disease.
- Other clinically significant, uncontrolled condition or disease.
- Use of any investigational drug within 30 days.
- Allergic to beta-2-agonists, inhaled corticosteroids or excipients.
- Positive pregnancy test.
- Using immunosuppressive medications.
- Milk protein allergy.
- Factors likely to interfere with attendance.
- Current smokers or ex-smokers with a history of >10 pack years.
- Affiliation wih Investigator site.
- Medications that may affect the course of asthma or interact with sympathomimetic amines.

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations: United Kingdom
GSK Investigational Site
Manchester, United Kingdom, M23 9QZ

United States, Wisconsin
GSK Investigational Site
Madison, Wisconsin, United States, 53792

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Sequence 1: FP, SFC, Placebo	Fluticasone Propionate (FP) 100 micrograms (mcg) twice daily (BID) in the first treatment period: Salmeterol/ Fluticasone Propionate Combination (SFC) 50/100 mcg BID in the second treatment period: Placebo in the third treatment period
Sequence 2: Placebo, SFC, FP	Placebo in the first treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the second treatment period: Fluticasone Propionate 100 mcg BID in the third treatment period
Sequence 3: SFC, FP, Placebo	Salmeterol/Fluticasone Propionate 50/100 Combination mcg BID in the first treatment period: Fluticasone Propionate 100 mcg BID in the second treatment period: Placebo in the third treatment period
Sequence 4: SFC, Placebo, FP	Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the first treatment period: Placebo in the second treatment period: Fluticasone Propionate 100 mcg BID in the third treatment period
Sequence 5: FP, Placebo, SFC	Fluticasone Propionate 100 mcg BID in the first treatment period: Placebo in the second treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the third treatment period
Sequence 6: Placebo, FP, SFC	Placebo in the first treatment period: Fluticasone Propionate 100 mcg BID in the second treatment period: Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID in the third treatment period

First Treatment Period

	Sequence 1: FP, SFC, Placebo	Sequence 2: Placebo, SFC, FP	Sequence 3: SFC, FP, Placebo	Sequence 4: SFC, Placebo, FP	Sequence 5: FP, Placebo, SFC	Sequence 6: Placebo, FP, SFC
Started	4	4	4	3	4	4
Completed	4	4	4	3	4	4
Not Completed	0	0	0	0	0	0

Second Treatment Period

	Sequence 1: FP, SFC, Placebo	Sequence 2: Placebo, SFC, FP	Sequence 3: SFC, FP, Placebo	Sequence 4: SFC, Placebo, FP	Sequence 5: FP, Placebo, SFC	Sequence 6: Placebo, FP, SFC
Started	4	4	4	3	4	4
Completed	4	4	4	3	3	4
Not Completed	0	0	0	0	1	0

	Sequence 1: FP, SFC, Placebo	Sequence 2: Placebo, SFC, FP	Sequence 3: SFC, FP, Placebo	Sequence 4: SFC, Placebo, FP	Sequence 5: FP, Placebo, SFC	Sequence 6: Placebo, FP, SFC
Withdrawal by Subject	0	0	0	0	1	0

Third Treatment Period

	Sequence 1: FP, SFC, Placebo	Sequence 2: Placebo, SFC, FP	Sequence 3: SFC, FP, Placebo	Sequence 4: SFC, Placebo, FP	Sequence 5: FP, Placebo, SFC	Sequence 6: Placebo, FP, SFC
Started	4	4	4	3	3	4
Completed	4	4	4	3	3	4
Not Completed	0	0	0	0	0	0

Baseline Characteristics

Reporting Groups

	Description
Overall Study Population	Overall Study Population: participants in all three treatment periods

Baseline Measures

	Overall Study Population
Number of Participants	23
Age, Continuous [units: years] Mean (Standard Deviation)	36.6 (6.63)
Gender, Male/Female [units: participants]	
Female	9
Male	14
Race/Ethnicity, Customized [units: participants]	
African American	2
Caucasian	21

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Weighted Mean Change From Baseline Over 0-6 Hours in Blood Eosinophils Post-Allergen Challenge on Day 35
Measure Description	Number of peripheral blood eosinophils measured from blood draws
Time Frame	0-6 hours post allergen challenge, 10-11 hours post treatment, Day 35
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: All participants receiving at least one dose of study medication who had at least one post-randomization efficacy assessment

Reporting Groups

	Description
Placebo	Placebo
FP 100 mcg BID	Fluticasone Propionate (FP) 100 mcg BID
SFC 50/100 mcg BID	Salmeterol/Fluticasone Propionate Combination (SFC) 50/100 mcg BID

Measured Values

	Placebo	FP 100 mcg BID	SFC 50/100 mcg BID
Number of Participants Analyzed	22	22	22
Weighted Mean Change From Baseline Over 0-6 Hours in Blood Eosinophils Post-Allergen Challenge on Day 35 [units: Giga Units per Liter (GI/L)] Mean (95% Confidence Interval)	-0.050 (-0.072 to -0.029)	-0.040 (-0.061 to -0.019)	-0.023 (-0.044 to -0.001)

2. Secondary Outcome Measure:

Measure Title	Weighted Mean Change From Baseline Over 0-6 Hours in Blood Eosinophils Post-Allergen Challenge on Day 14
Measure Description	Number of peripheral blood eosinophils measured from blood draws
Time Frame	0-6 hours, post allergen challenge, 1 hour post treatment, Day 14
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Placebo	Placebo
FP 100 mcg BID	Fluticasone Propionate (FP) 100 mcg BID
SFC 50/100 mcg BID	Salmeterol/Fluticasone Propionate Combination (SFC) 50/100 mcg BID

Measured Values

	Placebo	FP 100 mcg BID	SFC 50/100 mcg BID
Number of Participants Analyzed	21	23	20
Weighted Mean Change From Baseline Over 0-6 Hours in Blood Eosinophils Post-Allergen Challenge on Day 14 [units: Giga Units per Liter (GI/L)] Mean (95% Confidence Interval)	-0.023 (-0.039 to -0.006)	-0.022 (-0.038 to -0.007)	-0.013 (-0.029 to -0.004)

3. Secondary Outcome Measure:

Measure Title	Weighted Mean Change From Baseline Over 0-6 Hours in Serum IL-5 Post-Allergen Challenge on Day 35
Measure Description	Amount of serum interleukin (IL)-5 measured from blood draws
Time Frame	0-6 hours post allergen challenge, 10-11 hours post treatment, Day 35
Safety Issue?	No

Outcome Measure Data Not Reported

4. Secondary Outcome Measure:

Measure Title	Weighted Mean Change From Baseline Over 0-6 Hours in Serum IL-5 Post-Allergen Challenge on Day 14
Measure Description	Amount of serum IL-5 measured from blood draws
Time Frame	0-6 hours post allergen challenge, 1 hour after dosing, Day 14
Safety Issue?	No

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Placebo	Placebo
FP 100 mcg BID	Fluticasone Propionate 100 mcg BID
SFC 50/100 BID	Salmeterol/Fluticasone Propionate Combination 50/100 mcg BID

Serious Adverse Events

	Placebo	FP 100 mcg BID	SFC 50/100 BID
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Infections and infestations			
Appendicitis [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Placebo	FP 100 mcg BID	SFC 50/100 BID
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	14/22 (63.64%)	16/23 (69.57%)	10/22 (45.45%)
Blood and lymphatic system disorders			
Lymphadenopathy [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Eye disorders			
Eye pruritus [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Gastrointestinal disorders			
Abdominal pain upper [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)

	Placebo	FP 100 mcg BID	SFC 50/100 BID
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Diarrhea [A] †	1/22 (4.55%)	1/23 (4.35%)	0/22 (0%)
Nausea [A] †	1/22 (4.55%)	1/23 (4.35%)	0/22 (0%)
Toothache [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
General disorders			
Chest discomfort [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Discomfort [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Immune system disorders			
House dust allergy [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Hypersensitivity [A] †	0/22 (0%)	1/23 (4.35%)	1/22 (4.55%)
Multiple allergies [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Infections and infestations			
Appendicitis [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Candidiasis [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Lower respiratory tract infection [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Nasopharyngitis [A] †	2/22 (9.09%)	3/23 (13.04%)	2/22 (9.09%)
Sinusitis [A] †	0/22 (0%)	1/23 (4.35%)	1/22 (4.55%)
Tooth abscess [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Injury, poisoning and procedural complications			
Muscle strain [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Periorbital haematoma [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Post procedural complication [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Musculoskeletal and connective tissue disorders			
Pain in extremity [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)

	Placebo	FP 100 mcg BID	SFC 50/100 BID
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Tendonitis [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Nervous system disorders			
Headache [A] †	7/22 (31.82%)	3/23 (13.04%)	2/22 (9.09%)
Nerve compression [A] †	1/22 (4.55%)	0/23 (0%)	0/22 (0%)
Respiratory, thoracic and mediastinal disorders			
Dry Throat [A] †	0/22 (0%)	1/23 (4.35%)	1/22 (4.55%)
Dysphonia [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Dyspnoea [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Pharyngeal disorder [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Pharyngolarngeal Pain [A] †	1/22 (4.55%)	2/23 (8.7%)	2/22 (9.09%)
Productive cough [A] †	0/22 (0%)	1/23 (4.35%)	1/22 (4.55%)
Rhinorrhea [A] †	1/22 (4.55%)	0/23 (0%)	1/22 (4.55%)
Sinus congestion [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Sneezing [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)
Throat irritation [A] †	1/22 (4.55%)	2/23 (8.7%)	0/22 (0%)
Skin and subcutaneous tissue disorders			
Rash [A] †	0/22 (0%)	0/23 (0%)	1/22 (4.55%)
Surgical and medical procedures			
Tooth extraction [A] †	0/22 (0%)	1/23 (4.35%)	0/22 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Official Title: GSK Response Center
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