

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: SB-207499/125	
Title: A Randomized, 12-Week, Double-blind, Placebo-controlled, Parallel-group Pilot Study to Evaluate the Safety and Additional Efficacy of Adding a New Chemical Entity (NCE) to Treatment with ADVAIR 250/50 Twice Daily in Patients with Chronic Obstructive Pulmonary Disease (COPD).	
Rationale: The purpose of this study was to provide safety data to support the administration of a NCE and fluticasone propionate/salmeterol combination (FSC) in combination to subjects with moderate to severe COPD. Safety data for the SFC/placebo group are included in this summary. Results for the SFC/NCE groups will be added, if and when the NCE is approved and marketed.	
Phase: IIIb	
Study Period: 27 December 2002 to 23 January 2004.	
Study Design: A multicenter, randomized, double-blind, placebo-controlled study consisting of a 4-week, open-label, FSC run-in period, a 12-week treatment period, and a 1-week safety follow-up period.	
Centers: 41 centers in the United States.	
Indication: COPD.	
Treatment: Throughout the 4-week run-in and 12-week active treatment periods, all subjects were treated with FSC 250/50mcg twice daily (BID). At the end of the run-in period, subjects were randomized to receive either NCE or placebo in addition to FSC. A dose titration scheme was followed where, for the first 2 weeks of treatment, NCE or placebo was taken once daily. Thereafter, for the remaining 10 weeks of treatment, NCE or placebo was taken BID. Canisters of albuterol and/or nebulas were provided for on-demand use during the study.	
Objectives: The primary objective was to determine the safety of administering NCE in combination with FSC in subjects with moderate to severe COPD.	
Primary Outcome/Efficacy Variable: Safety.	
Secondary Outcome/Efficacy Variable(s): There were no secondary efficacy variables.	
Statistical Methods: The Intent-to-Treat (ITT) population was used for all safety analyses. The ITT population was defined as all randomized subjects who received at least 1 dose of study drug.	
Study Population: Male and non-pregnant female subjects using adequate contraception were eligible if they: had an established clinical history of COPD; were aged ≥ 40 years; had a current or prior history of at least 20 pack-years of cigarette smoking; and had a Baseline FEV ₁ $\geq 30\%$ and $\leq 70\%$ of predicted normal value and FEV ₁ /FVC ratio of $\leq 70\%$ at screening. Subjects were excluded from the study if they: had a current diagnosis of asthma; used any of the following respiratory medications during the study: long-acting beta-agonists, anticholinergics (inhaled and oral), cromolyn or nedocromil therapy, theophylline, leukotriene modifiers, and corticosteroid therapy; had clinically significant orthostatic changes in blood pressure or heart rate at Visit 1 or 2 (decrease in systolic blood pressure of ≥ 20 mmHg, or a decrease in diastolic blood pressure of ≥ 10 mmHg or an increase in heart rate of ≥ 10 beats/minute); were undergoing pulmonary rehabilitation; required a continuous positive airway pressure device for COPD or sleep apnea; or had any significant concurrent diseases that would place the subject at risk, interfere with clinical evaluations, or influence study participation.	
	FSC + Placebo
Number of Subjects:	
Planned, N	150
Randomized, N	164
Completed, n (%)	144 (88)
Total Number Subjects Withdrawn, n (%)	20 (12)
Withdrawn due to Adverse Events, n (%)	4 (2)
Withdrawn due to Lack of Efficacy, n (%)	0
Withdrawn for Other Reasons, n (%)	16 (10)
Demographics	
N (ITT)	164
Females: Males	77: 87
Mean Age, years (standard deviation [SD])	63.9 (9.04)
White, n (%)	140 (85)

Safety Results: ITT Population - Adverse events (AEs) and serious adverse events (SAEs) were reported from Visit 1 (screening) through to study completion (Final safety evaluation visit). Safety data for the SFC + placebo group are included in this summary. Results for the SFC + NCE groups will be added, if and when the NCE is approved and marketed.	
	FSC + Placebo (N=164)
Most Frequent Adverse Events – On-Therapy Run-in Period	n (%)
Subjects with any AE(s), n (%)	70 (43)
Headache	24 (15)
Dry mouth	5 (3)
Nasopharyngitis	5 (3)
Pharyngolaryngeal pain	5 (3)
Dizziness	4 (2)
Arthralgia	3 (2)
Back pain	3 (2)
Sinusitis	3 (2)
Tremor	3 (2)
Chest pain	2 (1)
Dyspepsia	2 (1)
Epistaxis	2 (1)
Fatigue	2 (1)
Hoarseness	2 (1)
Influenza	2 (1)
Insomnia	2 (1)
Nasal congestion	2 (1)
Nervousness	2 (1)
Sinus congestion	2 (1)
Sinus headache	2 (1)
Throat irritation	2 (1)
Most Frequent Adverse Events – On-Therapy Double-blind Period	n (%)
Subjects with any AE(s), n (%)	109 (66)
Headache	26 (16)
Nasopharyngitis	13 (8)
Pharyngolaryngeal pain	13 (8)
Back pain	10 (6)
Diarrhea	10 (6)
Constipation	9 (5)
Nausea	7 (4)
Arthralgia	6 (4)
Dizziness	6 (4)
Muscle cramp	6 (4)
Pain in extremity	6 (4)
Cough	5 (3)
Hoarseness	5 (3)
Serious Adverse Events - On-Therapy in the pre-vaccination phase n (%) [n considered by the investigator to be related to study medication]	
	FSC (N=398)
Screen failure subjects in Run-in Period	n (%)
Subjects with non-fatal SAEs, n (%)	5 (1)
	n (%) [related]
Atelectasis	1 (<1) [0]
Bronchial carcinoma	1 (<1) [0]
Chronic obstructive airways disease exacerbated	1 (<1) [0]
Hip fracture	1 (<1) [0]

Pneumonia	1 (<1) [0]
Pneumothorax	1 (<1) [0]
Pulmonary mass	1 (<1) [0]
Subjects with fatal SAEs, n (%)	0
	FSC + Placebo (N=164)
Double-blind Period	n (%)
Subjects with non-fatal SAEs, n (%)	3 (2)
	n (%) [related]
Chest discomfort	1 (<1) [0]
Chest pain	1 (<1) [0]
Chronic obstructive airways disease exacerbated	1 (<1) [0]
Hypoxia	1 (<1) [0]
Myocardial infarction	1 (<1) [0]
Pain in extremity	1 (<1) [0]
Upper respiratory tract infection	1 (<1) [0]
Subjects with fatal SAEs, n (%)	0

Conclusion:

During the run-in period, AEs were reported by 70 (43%) subjects randomized to FSC + placebo. The most frequently reported AE was headache. During the double-blind period, AEs were reported by 109 (66%) subjects in the FSC + placebo group. The most frequently reported AEs were headache, nasopharyngitis, and pharyngolaryngeal pain. Five (1%) subjects reported SAEs during the run-in period; none were reported by more than 1 subject and none were fatal. Three (2%) subjects in the FSC + placebo group reported SAEs during the double-blind period; none were reported by more than 1 subject. No fatal SAEs were reported.

Publications:

No Publications

Date Updated: 15-Mar-2006