

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: SCO100807	
Title : Randomised, open label, two period, crossover study to compare the steroid systemic exposure of Fluticasone Propionate (FP) from FP/Salmeterol (SALM) (500/50) DISKUS and Budesonide (BUD) from BUD/formoterol (FOR). (200/6) Turbuhaler in patients with severe Chronic Obstructive Pulmonary Disease.	
Rationale: The aims of the study were to compare the pharmacokinetics of the steroid components of FP/SALM DISKUS and BUD/FOR Turbuhaler at their clinically relevant doses in severe chronic pulmonary obstructive disease (COPD).	
Phase: I.	
Study Period: 19 July 2004 to 23 June 2005.	
Study Design: Randomised, open label, two period crossover study in subjects with severe COPD.	
Centres: One centre in Berlin, Germany and one centre in Llantrisant, United Kingdom.	
Indication: None.	
<p>Treatment: There was a 2-week run in period during which subjects were randomised to receive one of the following treatments:</p> <ul style="list-style-type: none"> • SALM 50 µg via the DISKUS, one inhalation twice daily (b.i.d.), or, • FOR 6 µg via the Turbuhaler, two inhalations b.i.d. <p>Those subjects already taking a long-acting β-agonist were converted to either SALM or FOR according to the randomisation schedule. Those subjects already taking combination therapy containing either FP or BUD had their existing therapy discontinued during the run-in period when the steroid component of their therapy was substituted with beclomethasone 400 µg b.i.d. for the duration of the run-in period. Following this, there were two treatment periods, each of 5–7 days duration (depending on whether the fifth day fell at the weekend). Subjects were randomised to receive 57 days of treatment with the licensed doses of each of the following:</p> <ul style="list-style-type: none"> • FP/SALM (500/50) DISKUS one inhalation b.i.d. • BUD/FOR (200/6) Turbuhaler two inhalations b.i.d. <p>Blood samples were collected after morning and evening dosing on one of Days 5–7 in each period. Following this day of pharmacokinetic sampling in Period 1 (Day 57) s subjects crossed-over and received the dose for Period 2, starting the next day. A follow up visit was conducted 4–10 days after the pharmacokinetic sampling day of the second period.</p>	
Objectives: To compare the exposure of the inhaled steroid FP and BUD following repeat dosing with SALM/FP DISKUS (500/50) one inhalation b.i.d. when compared with BUD/FOR Turbuhaler (200/6) two inhalations b.i.d. in a severe COPD population.	
<p>Statistical Methods: The primary endpoint was the pharmacokinetic parameter AUC(0-24), the area under concentration-time curve over the a.m. and p.m. dose intervals. The primary comparison was plasma FP AUC(0-24) versus BUD AUC(0-24). Following loge-transformation of the data, a mixed model was fitted, adjusting for the fixed effects treatment group, period and sequence with subject fitted as a random effect.</p> <p>The secondary comparisons were plasma FP versus BUD for AUC(0-12), AUC(12-24), Cmax (a.m.) and Cmax (p.m.). In addition an exploratory analysis of comparisons between AUC(0 12) versus AUC(12-24) and Cmax (a.m.) vs. Cmax (p.m.) was conducted for both FP and BUD individually.</p>	
Study Population: Chronic pulmonary obstructive disorder patients, aged 40-75 years inclusive, defined as either Stage III to Stage IV COPD diagnosis according to GOLD criteria (Global Strategy for the Diagnosis, Management, and Prevention of COPD).	
Number of Subjects:	
Planned N	20

Randomised N	16			
Completed n (%)	14 (88)			
Total Number Subjects Withdrawn N (%)	2 (13)			
Withdrawn due to Adverse Events n (%)	1 (6)			
Withdrawn for Other Reasons n (%)	1 (6)			
Demographics				
N (all subjects)	16			
Females: Males	2 : 14			
Median Age in Years (range)	58.0 (47- 1)			
Mean Weight in Kg (range)	79.70 (49.2, 99.1)			
White n (%)	16 (100)			
Pharmacokinetics Endpoints: A summary of geometric mean (95% confidence interval) derived pharmacokinetic parameters is presented in the following table.				
Parameter (units)	Geometric mean (95% confidence interval)			
	FP/SALM (500/50) (N=14)	BUD/FOR (400/12) (N=14)		
AUC(0-24) (pg.h/mL)	1123.4 (952.5, 1324.9)	5065.6 (4138.2, 6200.9)		
AUC(0-12) (pg.h/mL)	554.4 (464.9, 661.1)	2684.9 (2135.5, 3375.6)		
AUC(12-24) (pg.h/mL)	567.0 (482.2, 666.8)	2315.8 (1842.7, 2910.2)		
Cmax (a.m.) (pg/mL)	84.47 (70.56, 101.14)	782.35 (555.18, 1102.47)		
Cmax (p.m.) (pg/mL)	72.21 (61.15, 85.28)	646.61 (484.26, 863.38)		
tmax (a.m.) (pg/mL) ^a	1.00 (0.50–2.00)	0.17 (0.08–1.50)		
tmax (p.m.) (pg/mL) ^a	1.00 (0.50–2.00)	0.15 (0.08–1.50)		
^a Median (range)				
A summary of the statistical comparison of FP and BUD pharmacokinetic parameters is presented in the following table:				
Comparison	Adjusted Geom. Mean FP	BUD	Ratio	90% CI
FP AUC(0-24) :BUD AUC(0-24) (pg.h/mL)	1106.85	5092.11	0.22	(0.18, 0.26)
FP AUC(0-12) :BUD AUC(0-12) (pg.h/mL)	547.19	2727.23	0.20	(0.17, 0.24)
FP AUC(12-24) :BUD AUC(12-24) (pg.h/mL)	557.75	2298.92	0.24	(0.20, 0.30)
FP Cmax (a.m.): BUD Cmax (a.m.) (pg/mL)	83.75	803.13	0.10	(0.08, 0.13)
FP Cmax (p.m.): BUD Cmax (p.m.) (pg/mL)	71.19	649.47	0.11	(0.08, 0.14)
Adjusted Geom. Mean = adjusted geometric mean, BUD = budesonide, CI = confidence interval				
A summary of statistical comparison of pharmacokinetic parameters following morning and evening dosing for FP and BUD is presented in the following table:				
Comparison	Adjusted Geom. Mean a.m.	p.m.	Ratio	90% CI
FP AUC(0-12) : FP AUC(12-24) (pg.h/mL)	546.25	558.71	0.98	(0.92, 1.04)
FP Cmax (am) : FP Cmax (p.m.) (pg/mL)	83.51	71.39	1.17	(1.08, 1.27)
BUD AUC(0-12) : BUD AUC(12-24) (pg.h/mL)	2696.12	2325.45	1.16	(0.99, 1.36)
BUD Cmax (a.m.) : BUD Cmax (p.m.) (pg/mL)	794.42	656.58	1.21	(1.00, 1.47)
Adjusted Geom. Mean = adjusted geometric mean, BUD = budesonide, CI = confidence interval				
Safety results: Serious adverse events only were collected during the screening and run-in period. All adverse events were collected from Day 1 to follow-up.				
Adverse Events:	FP/SALM n of subjects (%)	BUD/FOR n of subjects (%)		
N (all subjects)	16	15		
No. subjects with adverse events n (%)	1 (6)	5 (33)		
Most Frequent adverse events				
Headache	0	3 (20)		
Cough	0	2 (13)		
Serious Adverse Events:				
N (all subjects)	16	15		

No. subjects with serious adverse event n (%)	1 (6)	0
Atrial fibrillation	1 (6)	0

Publications: No publication.

Date updated: 14-Feb-2006