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: SSD113434

Title : A randomised, double-blind, placebo-controlled study of topical GW870086X formulation in subjects with moderate or severe atopic dermatitis.

Rationale: The purpose of the study was to assess the anti-inflammatory activity and tolerability of GW870086X when administered as a topical agent to the skin of subjects suffering from atopic dermatitis.
One of the adverse effects of long term treatment of glucocorticoid steroids is suppression of the HPA axis. Hitherto, the studies conducted in healthy subjects have showed no significant suppression of the HPA axis even at levels of systemic exposure that are associated with complete inhibition of endogeneous cortisol production after administration of non-selective glucocorticosteroids.
GW870086X is 3-5 times less potent than fluticasone propionate (FP) based on pre-clinical data. The therapeutic dose for FP cream is 0.05% and therefore a concentration of 0.2% GW870086X cream was expected to exhibit similar efficacy to FP. The higher dose of 2% was selected to provide safety cover for future studies and to investigate whether GW870086X cream had efficacy in this indication had the 0.2% cream shown no effect.

Phase: II

Study Period: 13 December 2010 – 14 April 2011

Study Design: Randomised, double-blind, placebo controlled

Centres: One centre in Berlin, Germany.

Indication: Atopic dermatitis.

Treatment: Subjects were assigned to take 3 out of the 4 possible treatments for 21±2 days: GW870086X 0.2% cream, GW870086X 2% cream, FP 0.05% cream (as a positive control) and placebo cream. Each of the 3 assigned treatments was administered concurrently but on different lesions (the same lesion was used for each treatment throughout the study period). Blood samples were taken on Days 7, 14 and 21 for pharmacokinetic assessment. Local irritancy was assessed on Days 1-3. On Days 4-21 subjects applied the cream to their lesions at home. Subjects attended the unit on Days 7±2 14±2, 21±2 and 22±2 for review of their lesions using the Three Item Severity (TIS) scale. TIS score was the sum of the three symptom scores (erythema, oedema/papulation, and excoriation) using a score of 0-3 leading to a 0-9 range lesion.
Follow up was approximately 7-14 days after the last dose.
The total duration of the study was 22 days plus screening and follow up.

Objectives: To investigate the efficacy of GW870086X cream (0.2% and 2%) applied once daily for 21 days on diseased skin of adult subjects with atopic dermatitis using the TIS scale on Day 22.

Statistical Methods: All randomised subjects with at least one post-dose TIS assessment were included in the statistical model. The change from baseline in the TIS scale between GW870086X (0.2% and 2%) versus placebo was analysed by mixed model repeated measures (MMRM) analysis, with the primary inference being the change at Day 22.

Study Population: Adult subjects aged 18–65 years inclusive with moderate to severe atopic dermatitis as defined by a score of >25 using the modified SCORing Atopic Dermatitis (SCORAD) rating scale and having at least 3 index lesions ($\geq$ 1cm^2 in size) with a sum score of $\geq$4 and $\leq$6 for erythema, oedema/papulation and excoriations using the Three Item Severity (TIS) rating scale. Subjects with a body weight $\geq$50 kg and body mass index within the range 19.0–29.0 kg/m2 inclusive. Subjects with atopic dermatitis restricted to the face, the feet and/or the hands only were excluded.

Number of Subjects:	**X N=10**	**Y N=5**	**Z N=10**	**Total N= 25**
Planned N	10	5	10	25
Randomised N	10	5	10	25
Completed n (%)	10 (100)	5 (100)	10 (100)	25 (100)
Number of Subjects Included in All Subjects (Safety) Population, n (%)	10 (100)	5 (100)	10 (100)	25 (100)
Number of Subjects Completed in PK Population, n (%)	10 (100)	5 (100)	10 (100)	25 (100)
Total Number of Subjects Withdrawn N (%)	0	0	0	0
Demographics	**X N=10**	**Y N=5**	**Z N=10**	**Total N=25**
N (ITT)	10	5	10	25
Females: Males	3:7	2:3	1:9	6:19

Mean Age in Years (sd)	41.9 (18.81)	40.8 (19.43)	28.3 (10.15)	36.2 (16.68)
Mean Body Mass Index in Kg/m^2 (sd)	24.84 (2.21)	24.34 (3.29)	24.08 (3.12)	24.44 (2.72)
Mean Weight in Kg (sd)	76.9 (10.03)	74.4 (12.54)	77.5 (14.74)	76.6 (12.12)
Mean Height in cm (sd)	175.7 (8.86)	174.8 (12.46)	178.9 (8.46)	176.8 (9.24)
Mean SCORing Atopic Dermatitis (SCORAD) Score (sd)	34.5 (7.25)	32.4 (7.7)	42.2 (6.41)	37.2 (7.95)
Not Hispanic or Latino n (%)	10 (100)	5 (100)	10 (100)	25 (100)
White – Caucasion/European n (%)	10 (100)	5 (100)	10 (100)	25 (100)

Efficacy

Efficacy: Summary of Results from Statistical Analysis of TIS Change From Baseline Scores by Day presented below.

Treatment	N	Planned day[1]	n	Adjusted Means (SE)	95% CI
GW870086 0.2%	20	2	20	-0.37 (0.190)	(-0.75, 0.02)
		3	20	-0.91 (0.266)	(-1.44, -0.38)
		7	20	-1.43 (0.363)	(-2.15, -0.70)
		14	20	-1.82 (0.367)	(-2.55, -1.09)
		22	20	-1.99 (0.418)	(-2.82, -1.15)
GW870086 2%	15	2	15	-0.53 (0.203)	(-0.94, -0.12)
		3	15	-0.80 (0.291)	(-1.38, -0.22)
		7	15	-1.78 (0.403)	(-2.58, -0.98)
		14	15	-2.23 (0.408)	(-3.04, -1.42)
		22	15	-2.49 (0.465)	(-3.42, -1.56)
Placebo	25	2	25	-0.45 (0.181)	(-0.82, -0.09)
		3	25	-0.94 (0.246)	(-1.43, -0.45)
		7	25	-1.19 (0.331)	(-1.85, -0.53)
		14	25	-1.58 (0.335)	(-2.25, -0.91)
		22	25	-1.61 (0.380)	(-2.36, -0.85)
FP 0.05%	15	2	15	-0.62 (0.203)	(-1.03, -0.22)
		3	15	-1.22 (0.292)	(-1.80, -0.64)
		7	15	-2.47 (0.405)	(-3.28, -1.67)
		14	15	-2.97 (0.409)	(-3.78, -2.15)
		22	15	-3.11 (0.467)	(-4.05, -2.18)

1. Days 7, 14 and 22 can occur +/- 2days

The adjusted change from baseline means were calculated by fitting a mixed effects repeated measures model fitting subject level baseline, lesion level baseline, lesion level baseline by time and treatment by time as fixed effects with subject fitted as a random effect and time as a repeated effect. A negative response indicates an improvement in the average change from baseline TIS score.

The difference in adjusted means provides an estimate of the difference in the mean TIS scores between the test and the reference arms as displayed along with the 95% CI of the difference and p-value.

Pharmacokinetics (PK)

Twenty-five subjects were included in the pharmacokinetic population. GW870086X plasma concentrations were not quantifiable (<40pg/mL) at any time-point in 22 of the 25 subjects up to 24 h post-dose on Day 21. Only 3 subjects treated with sequence X (GW870086X 0.2%, GW870086X 2% and placebo) had single quantifiable values ranging from 51.1 to 55.0 pg/mL.

Safety results: Adverse event and serious adverse event (SAE) data were recorded from the start of investigational product and until the follow-up contact. Any SAEs related to study participation or related to a GSK concomitant medication were to be recorded from the time a subject consented to participate in the study up to and including the follow-up contact.
No subject experienced a serious AE (SAE) or withdrew due to an AE during this study. All reported AEs are summarised below. Of note is one patient who reported an incidence of tachycardia of 31 minutes duration, 12 hours and 51 minutes after their Day 9 dose. This event was not considered to be related to study drug. No intervention or follow up was required.

Adverse Events:	**X N=10**	**Y N=5**	**Z N=10**	**Total N=25**
N (ITT)	10	5	10	25
No. subjects with AEs n (%)	6 (60)	2 (40)	5 (50)	13

No. subjects with AEs related to investigational product n (%)	0	0	0	0
Most Frequent AEs				
Headache	2 (20)	0	2 (20)	4 (16)
Dizziness	0	2 (40)	0	2 (8)
Dermatitis atopic	1 (10)	0	1 (10)	2 (8)
Nasopharyngitis	1 (10)	0	0	1 (4)
Arthralgia	1 (10)	0	0	1 (4)
Intervertebral disc protrusion	1 (10)	0	0	1 (4)
Tachycardia	1 (10)	0	0	1 (4)
Gastroenteritis norovirus	0	0	1 (10)	1 (4)
Confusion	0	0	1 (10)	1 (4)
Oropharyngeal pain	0	0	1 (10)	1 (4)

X = GW870086X 0.2% cream; GW870086X 2% cream; Placebo cream
Y = Placebo cream; GW870086X 2% cream; FP 0.05% cream
Z = GW870086X 0.2% cream; Placebo cream; FP 0.05% cream