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.

GSK Medicine: 0.05% Clobetasone Butyrate Cream

Study Number: 111187

Title: Multi-center, Randomised, Double-blind, Parallel, Placebo Controlled Study Of 0.05% Clobetasone Butyrate Cream in Subjects with Eczema to evaluate the Efficacy and Safety

Rationale: The purpose of the study was to evaluate clinical efficacy and safety of 0.05% Clobetasone Butyrate cream so as to introduce this drug in China in compliance with Chinese drug registration regulation (Registration category 3.1). Efficacy of 0.05% Clobetasone Butyrate cream was compared to a Placebo (cream base) based on EASI scores (The Eczema Area and Severity Index), IGA score (Investigators Global Assessment Scale), VAS (Visual Analog Scale) Method and subject based disease control assessments after treatment.

Phase: Phase III

Study Period: 28 Feb 2008 to 10 Feb 2009

Study Design: This was a multi-centre, randomised, double-blind, parallel, placebo controlled study. Screening examinations were performed within 3 days before administration study medication for subjects with eczema between 12 and 65 years of age. Eligible subjects were randomised into two parallel groups receiving test or placebo treatment with repeat applications, twice daily for a study period of 14 days. Subjects recorded subject diary daily and visited the site at Day 7 and 14 respectively.

Centres: 8 centres (China)

Indication: Eczema

Treatments:
Test: 0.05% Clobetasone Butyrate Cream
Control: Placebo (cream base)

Objectives: The objective of the study was to evaluate clinical efficacy and safety of 0.05% Clobetasone Butyrate Cream versus Placebo (cream base) applied to involved skin of subjects with eczema for 14 days.

Primary Efficacy Variable:

1. Changes from baseline in EASI score at Day 7 and Day 14
2. Percentage reduction of EASI at Day 14

Secondary Efficacy Variable(s):

1. Changes from baseline in IGA graded score at Day 7 and Day 14
2. Changes from baseline VAS score at Day 7 and Day 14
3. Subject-based assessment score of disease control at Day 7 and Day 14

Statistical Methods:
Efficacy variables were analysed using one-sided test, at a significance level of ≤0.05 with p value. Change from baseline to each post-dose assessment in EASI value on Day 7, 14 were analyzed using descriptive statistics. An ANCOVA model was used to compare the change of EASI score for two groups after 14 days treatment, the baseline EASI score as the covariate, treatment group and center effects were included.

Improvement of IGA from baseline; to compare the improvement of eczema symptoms pruritus (VAS method) from baseline; the score of a subject-based assessment of disease control. The IGA scores at 0, 7 and 14 days visit and the change from baseline after treatment were analyzed using descriptive statistics. Wilcoxon rank test was used to compare the change from baseline at different times between treatment groups, while signed rank sum test was used to compare the change from baseline at different times in each group.

Change in pruritis scores and subject's self-assessment of pruritus symptoms were analyzed using descriptive statistics. A t-test or Wilcoxon rank test was used to compare the change from baseline at different times between treatment groups.

Efficacy was determined for Full analysis set population defined as all subjects who were randomized into the study and received at least one dose of the study drug with at least one efficacy data after treatment. Safety set was used to evaluate safety and included all subjects enrolled into the study who received at least one dose of the study drug, had the safety evaluation data after receiving study drug.

Study Population:
Subjects aged 12 to 65 years, male or female, with moderate and above eczema as defined by a score ≥ 3 using the IGA of eczema severity.

	Clobetasone Butyrate Cream	Placebo Cream
Number of Subjects:		
Planned, N	100	100
Randomised, N	120	120
Completed, n (%)	113 (94.17)	109 (90.83)
Total Number Subjects Withdrawn, N (%)	7(5.83)	11(9.17)
Withdrawn due to Adverse Events n (%)	0(0)	1 (0.83)
Protocol Violation n (%)	0(0)	1 (0.83)
Lack of efficacy n (%)	4 (3.33)	8 (6.67)
Subject voluntary withdrawal n (%)	2 (1.67)	0 (0.00)
Withdrawn for other reasons n (%)	1 (0.83)	1 (0.83)
Demographics		
N (ITT)	119	119
Females: Males	73: 46	66: 53
Mean Age, years (SD)	41.90 (12.93)	41.89 (12.65)
Primary Efficacy Results: **1. Changes from baseline in EASI score at Day 7 and Day 14**		
Time-points	**Clobetasone Butyrate Cream**	**Placebo Cream**
Baseline, Mean(SD)	4.12(2.58)	4.09(2.70)
Day 7 treatment, Mean(SD)	2.47(2.41)	2.98(2.27)
Day 7 – Baseline, Mean(SD)	-1.64(1.57)	-1.11(1.90)
Day 14 of treatment, Mean(SD)	1.47(2.14)	2.31(2.23)
Day 14 – Baseline, Mean(SD)	-2.65(2.39)	-1.78(2.36)
Difference between treatments:		
	t test	**p value**
Day 7 - Baseline	-2.38	0.018
Day 14 - Baseline	-2.83	0.005
2. Percentage Reduction of EASI at Day 14		
14 day %Reduction, Mean(SD)	65.34 (34.47)	38.84 (48.45)
Difference between treatments:		
	F test	**p value**
Clobetasone Butyrate Cream vs Placebo Cream	24.01	<0.0001
Secondary Efficacy Results: **1. Changes from baseline in IGA graded score at Day 7 and Day 14**		
Time-points	**Clobetasone Butyrate Cream**	**Placebo Cream**
Baseline, Mean(SD)	3.24(0.47)	3.23(0.44)
Day 7 treatment, Mean(SD)	2.27(0.84)	2.76(0.76)
Day 7 – Baseline, Mean(SD)	-0.97(0.84)	-0.47(0.70)
Day 14 of treatment, Mean(SD)	1.50(1.21)	2.27(1.12)
Day 14 – Baseline, Mean(SD)	-1.75(1.19)	-0.96(1.09)
Difference between treatments:		
	Z value	**p value**
Day 7 - Baseline	-4.73	<0.0001
Day 14 - Baseline	-5.06	<0.0001
2. Changes from baseline in VAS score at Day 7 and Day 14		
Time-points	**Clobetasone Butyrate Cream**	**Placebo Cream**
Baseline, Mean(SD)	66.85(17.68)	67.61(20.21)
Day 7 treatment, Mean(SD)	30.41(25.78)	43.45(24.63)
Day 7 – Baseline, Mean(SD)	-36.44(28.15)	-24.15(24.68)
Day 14 of treatment, Mean(SD)	18.78(22.77)	35.38(27.02)

Day 14 – Baseline, Mean(SD)	-48.07(26.72)	-32.23(30.52)
Difference between treatments		
	t test	**p value**
Day 7 - Baseline	-3.58	0.0004
Day 14 - Baseline	-4.26	<0.0001
3. Subject-based assessment score of disease control* at Day 7 and Day 14		
Parameter	**Clobetasone Butyrate Cream**	**Placebo Cream**
Day 7		
0	5(4.20%)	1(0.84%)
1	45 (37.82%)	16 (13.45%)
2	44 (36.97%)	55 (46.22%)
3	25 (21.01%)	47 (39.50%)
Day 14		
0	38 (31.93%)	14 (11.76%)
1	38 (31.93%)	26 (21.85%)
2	28 (23.53%)	35 (29.41%)
3	15 (12.61%)	44 (36.97%)
Difference between treatments		
	Z value	**p value**
Day 7 during treatment	-4.66	<0.0001
Day 14 during treatment	-5.30	<0.0001
*Four point scale: 0 (complete disease control), 1 (good disease control), 2 (limited disease control), 3 (uncontrolled disease)		
Safety Results: An on therapy adverse event (AE) was defined as an AE with onset on or after the start date of study medication throughout the study period.		
	Clobetasone Butyrate Cream	**Placebo Cream**
Total number of subjects	119	119
Subjects with any AEs, n(%)	11 (9.24)	7 (5.88)
Most Frequent Adverse Events – On-Therapy	**n (%)**	**n (%)**
Urticaria	1(0.84)	0(0)
Rising liver enzyme levels	1(0.84)	3(2.52)
Rising Alanine transaminase levels	1(0.84)	0(0)
Rising Total Bilirubin	1(0.84)	0(0)
Rising urine glucose	1(0.84)	0(0)
Rising blood urea	1(0.84)	0(0)
Upper respiratory infection	1(0.84)	0(0)
Leukocytopenia	1(0.84)	0(0)
Rising eosinophils counts	1(0.84)	0(0)
Rising urine leukocyte counts	1(0.84)	0(0)
Hematuria	1(0.84)	0(0)
Local reactions	1(0.84)	0(0)
Pain	2(1.68)	1(0.84)
Serious Adverse Events (SAE) - On-Therapy: No SAEs were observed in the study		

Conclusion:
This study showed statistically significant difference between 0.05% Clobetasone Butyrate Cream and Placebo cream for all efficacy variables. The incidences of AEs were 9.24% and 5.88% in Clobetasone Butyrate Cream and Placebo Cream group respectively.