2. SYNOPSIS

Name of Company: Pierre Fabre Dermatologie	**Individual Study Table**	**(For National Authority Use Only)**
Name of finished product: DC115 GM 02A	**Referring to Module 5 of the Dossier**	
Name of active substance: Ciclopiroxolamine	**Vol.: .....Page: .....**	

Title of study:	Efficacy study of a ciclopiroxolamine 1% foam (DC 115 GM 02A) versus ciclopiroxolamine 1.5% shampoo (SEBIPROX®) in the treatment of moderate seborrheic dermatitis of the scalp.	
Investigator-Coordinator:	Dr Catherine QUEILLE-ROUSSEL	
Study centre(s):	CPCAD Hôpital L'Archet 2 151, route de St Antoine de Ginestière F-06202 Nice cedex 3	
Publication (reference):	NA	
Studied period *(years, months …)*: **(date of first enrolment) (date of last completed)**	06-Apr-2009 14-Dec-2009	**Phase of development:** Phase II
Objectives: **Primary:**	To assess the efficacy of a ciclopiroxolamine (CPO) 1% foam (DC 115 GM 02A) *versus* reference therapy CPO 1.5% shampoo (SEBIPROX®), on moderate seborrheic dermatitis of the scalp, after 4 weeks treatment.	
Secondary:	▪ To assess the efficacy of a CPO 1% foam (DC 115 GM 02A), on moderate of seborrheic dermatitis of the scalp, after 2 weeks treatment, ▪ To assess the local and general tolerance of DC 115 GM 02A foam, after 4 weeks treatment.	
Methodology:	Monocentre, intra-individual, half scalp randomised, Investigator masked, proof of concept study, DC 115 GM 02A foam (1% CPO) *versus* reference therapy SEBIPROX® shampoo (1.5% CPO).	
Number of patients (planned and analysed):	44 patients.	
Diagnosis and main criteria for inclusion:	Patients aged more than 18 years old with a stable or exacerbating moderate seborrheic dermatitis of the scalp (score of scaling and erythema between 2 to 4) comparable on both sides of the half scalp (sum score difference less or equal than 1 between both sides)	
Test product: **Dose:** **Mode of administration:** **Batch number:**	DC115 GM 02A (CPO 1% Foam) Daily application on half scalp (except Sundays) The foam was applied on the scalp, using gloved fingertips, a gentle massage was performed into the affected areas until the foam wetted the treated half scalp. The foam quantity had to be sufficient to completely cover the half scalp. It was left to dry naturally. The product was applied by a study personnel delegated by the approved Investigator, at the study centre. No application was performed on Sundays. CLP079	

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Reference therapy: **Dose:**	SEBIPROX® (CPO 1.5 % Shampoo). 3 applications per week on a half scalp, with a minimum of 1 day between 2 applications.
Mode of administration:	The hair of a half scalp was wetted. A sufficient SEBIPROX® shampoo was applied to produce an abundant lather. The affected area was vigorously massaged with the fingertips gloved, then the scalp was rinsed thoroughly and the procedure repeated a second time. The product was left on the hair 3 to 5 minutes. The product was applied by a study personnel delegated by the approved Investigator, at the study centre. No application was performed on Sundays.
Batch number:	991K
Associated Product:	Soft non treating shampoo.
Duration of treatment:	Treatment duration was 28 days ± 2 (4 weeks).
Criteria for evaluation: **Treatment effectiveness:**	The primary end-point was the sum score of seborrheic dermatitis, at Day 28. The Sum Score (SS) is defined as the sum of clinical symptoms of scaling and erythema. Each symptom was scored on a 6-point severity scale (0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = pronounced, 5 = severe).
Efficacy:	▪ The Sum Score (SS) of seborrheic dermatitis, at Day 14. The sum score is defined as the sum of clinical symptoms of scaling and erythema. Each symptom was scored on a 6 point severity scale (0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = pronounced, 5 = severe). ▪ Evaluation of clinical symptom of seborrheic dermatitis of the scalp on each half scalp (Scaling, Erythema) by the Investigator, at Day 14 and 28 using a 6-point severity scale. ▪ Itching (pruritus), the main subjective symptom of seborrheic dermatitis of the scalp was assessed by the Patient on each half scalp at Day 14 and 28 using a 6-point severity scale. ▪ Evolution of the status of seborrheic dermatitis on each half head, at Day 14 and 28 using a 6-point severity scale. ▪ Rate of cure of each half head assessed at Day 14 and 28, The cure is defined as a score of 0 (or 1 if baseline score ≥ 3) for each of the individual scores for "Status of seborrheic dermatitis", "Scaling" and "Erythema", each scored on a 6 point severity scale. ▪ Evolution of the scalp area affected on each half head, at Day 14 and 28. A 5-point area scale was used by the Investigator (0 = < 10%, 1 = ≥ 10% but < 30%, 2 = ≥ 30% but < 50%, 3 = ≥ 50% but < 70%, 4 = ≥ 70%). ▪ Investigator and Patient global efficacy assessment, choosing the best scalp improvement at Day 14 and 28.
Safety:	▪ Local tolerance of dryness, increased erythema, and increased seborrhoea were assessed by the Investigator at Day 14 and Day 28, according a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). ▪ The patient was asked to report any burning sensation, pain and increased itching after products application. This was scored accepting to a 4-point scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe).

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Statistical methods:	For the improvement of sum score, an ANCOVA was performed with sequence, side and treatment as fixed effect, patient as random effect and baseline as covariate. The normality of residuals was checked via the Shapiro-Wilk test. In case of non-normality, the improvement of sum score was analysed by the non-parametric method for cross-over design with sequence, patient, side and treatment factors proposed by G. KOCH. Each improvement of scores (scaling, erythema, itching), Investigator and patient local tolerance assessment, status of seborrheic dermatitis and scalp area score were analysed by the non-parametric method for cross-over design with sequence, patient, side and treatment factors proposed by G. KOCH. Investigator and patient global efficacy assessment, matched proportions for binary criteria were analysed by the non-parametric McNemar's test for patient's preference. The safety was only descriptive.

Summary - Conclusions:

Demographics

Forty-four (44) patients (22 males and 22 females) were randomized. The mean age was 40.38 ± 11.37 years.

Demographic data are summarized in the table 1 below.

Table 1 – Demographics

Study population (N=44)			
		N	**Percent**
Sex			
	Female	22	50.0%
	Male	22	50.0%
Age (Years)			
	Mean	40.38	
	SD	11.37	
	Median	37.65	
	[Min-Max]	[25.40 - 67.60]	

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Efficacy results

The results of the comparisons between DC115 GM 02A and SEBIPROX performed on the mean clinical scores are summarized in the table 2.

Table 2 – Mean change of the clinical scores at Day14 and Day28 and p-value

		DC115 GM 02A	**SEBIPROX**	p*
Clinical global sum score	Day14	-3.00	-3.02	NS
	Day28	-4.34	-4.80	NS
Erythema score	Day14	-1.39	-1.23	NS
	Day28	-1.82	-2.14	p<0.05
Scaling score	Day14	-1.61	-1.80	NS
	Day28	-2.52	-2.66	NS
Scalp area score	Day14	-1.41	-1.57	NS
	Day28	-2.07	-2.14	NS
Itching	Day14	-2.30	-2.26	NS
	Day28	-2.68	-2.73	NS
Status of SD	Day14	-1.11	-1.20	NS
	Day28	-1.82	-2.00	NS

The results of the comparisons between DC115 GM 02A and SEBIPROX performed on the percentages are summarized in the table 3.

Table 3 – Percentages at Day14 and Day28 and p-value

		DC115 GM 02A	**SEBIPROX**	p*
Rate of cure	Day14	22.7%	29.5%	NS
	Day28	45.5%	61.4%	p<0.05
Investigator global efficacy assessment	Day14	72.7%	70.5%	NS
	Day28	75.0%	88.6%	NS
Patient global efficacy assessment	Day14	76.7%	72.1%	NS
	Day28	84.1%	90.9%	NS

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In order to assess the efficacy of DC115 GM 02A versus SEBIPROX® on moderate seborrheic dermatitis of the scalp, 50 patients were screened and 44 were randomized. The 44 randomized patients (22 males and 22 females) completed the whole study. The mean age was 40.38 ± 11.37 years.
The main criterion was the mean clinical change in the Clinical Global Sum Score (CGSS) after 28 days of treatment.
The secondary objectives were the mean change from baseline of CGSS at Day14 and the mean change from baseline of clinical scores (erythema, scaling), subjective symptoms (itching), scalp area score, status of SD, rate of cure and global efficacy assessment (Investigator and Patient) at Day14 and Day28.
In the present study, the two tested products proved to be active. After 4 weeks of treatment, the global severity (expressed by the CGSS at Day28) decreased by more than 70% from the baseline for both treatments. An improvement of the CGSS was observed at Day14 as at Day28 for both treatments but no significant difference was detected between DC115 GM 02A and the reference product SEBIPROX® whatever the time point. For the SD signs, erythema and scaling assessed at Day14 and Day 28 also improved in both treated half-scalp. The comparisons between-treatments did not show any significant difference at Day14. However at Day28, a statistically significant difference was detected on erythema scores with a better improvement of this symptom on the half-scalp treated with SEBIPROX®.
Concerning the scalp area score, a decrease in the percentages of affected area was observed at Day14 and Day 28 for both treatments but no significant difference was detected between DC115 GM 02A and SEBIPROX®.
In the same way, an improvement of itching was also observed at Day14 and Day 28 in both treatments but the comparisons between DC115 GM 02A and SEBIPROX® performed at Day14 and Day28 did not show any statistically significant difference.
For the SD status, clinical scores attributed by the Investigator at Day14 and Day28 decreased for both treatments. However the mean change from baseline was not significantly different between DC115 GM 02A and SEBIPROX®.
About the rate of cure assessed by the Investigator, a significant difference was only detected at Day28 with a rate of cure more important on the half-scalp treated with SEBIPROX®.
Global efficacy assessment performed by both Investigator and Patient showed that the percentages of half-scalp most improved in each treatment category were not significantly different between DC115 GM 02A and SEBIPROX®.
A total of 37 TEAEs was reported in 25 patients during the study. The relationship to the study products was not excluded for 21 of all TEAEs.
Finally, the tested product was as well tolerated as the reference product SEBIPROX®. Among the not excluded TEAEs, only expected local reactions of mild intensity were reported by the patients.

Finally, the tested product DC115 GM 02A was as well tolerated as the reference product SEBIPROX®. Only expected local reactions of mild intensity were reported. The DC115 GM 02A foam efficacy does not significantly differ from the SEBIPROX® shampoo in the treatment of moderate seborrheic dermatitis of the scalp.

Date of report: 12-Oct-2010