Clinical Study Synopsis for Public Disclosure

The clinical study synopsis

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SYNOPSIS

Title of Study:
A multicenter, randomised, double blind, placebo-controlled study of efficacy, safety, and tolerability of Kaprolac® K301 for the treatment of seborrhoeic eczema (SE) of the scalp

Study Centre(s):
21 centres in Sweden

Publication (reference):
Not applicable

Studied period (years):
First patient enrolled 2008-02-11
Last patient completed 2008-04-14

Phase of development:
III

Objectives:
The primary objective of the study was to evaluate the efficacy of K301 compared to placebo after 4 weeks treatment in adults with SE of the scalp.

Secondary efficacy objectives were to evaluate the efficacy after 2 and 4 weeks of treatment with K301 compared to placebo and to assess safety and tolerability of K301 in adults with SE of the scalp.

Methodology:
This was a multicenter, randomised, double-blind, placebo-controlled study of efficacy, safety, and tolerability of K301 in adults with SE of the scalp. The patients were to be randomly allocated to treatment with K301 or to a matching placebo to be applied once daily for 4 weeks. Treatment was to be applied before bedtime and could be washed out with the patient's normal shampoo in the morning. Each patient was to undergo a baseline visit and two further visits after 2 and 4 weeks of treatment, followed by a telephone contact at week 5 for safety follow-up. The total duration of the patient's involvement in the study was to be 5 weeks.

Number of patients (planned and analysed):

	Placebo	K301	Total
No. planned:	60	120	180
No. randomised:	65	136	201
No. analysed for safety:	64	136	200
No. analysed for efficacy:	64	134	198
No. completed:	63	132	195

Diagnosis and main criteria for inclusion:
The following entry criteria applied:

- Male or female (including fertile women)
- 18-70 years of age
- SE of the scalp for at least 2 months
- Presenting erythema and desquamation of mild to moderate intensity
- Signed written informed consent

Test product, dose and mode of administration, batch number (no):
K301 (batch no: S-MD71203) was to be applied once daily to the scalp before bedtime during the 4-week treatment period and could be washed out with the patient's normal shampoo in the morning. The test product K301 was composed of the active substances propylene glycol, urea and lactic acid together with the excipients glycerol and water.

Duration of treatment:
Four weeks

Reference therapy, dose and mode of administration, batch number:
Placebo (batch no: S-MD71204) was to be applied once daily to the scalp before bedtime during the 4-week treatment period and could be washed out with the patient's normal shampoo in the morning. The placebo solution was identical in appearance to K301 and contained water with small amounts of glycerol, isopropanol and a preservative.

Criteria for evaluation:
Efficacy
Erythema and desquamation scores were to be rated by the Investigator at baseline, and after 2 and 4 weeks of treatment. The primary efficacy endpoint was the sum of erythema and desquamation scores at Week 4. The intensity rating of erythema and desquamation was standardised by the use of descriptive scales as follows:

Erythema score
A target lesion was to be selected on the basis of the most severe symptoms.

0 Absent (no erythema or barely visible: pale or pink)
1 Slight (erythema is slightly visible or just visible: light red)
2 Mild (erythema is visible: red)
3 Moderate (erythema is clearly visible: red)
4 Pronounced (erythema is clearly visible: clear red)
5 Severe (brisk erythema: clear red-violet red, dark red)

Desquamation score
A target lesion was to be selected on the basis of the most severe symptoms.

0 Absent (no desquamation)
1 Slight (desquamation), small loose flakes as a course, white or greyish powder
2 Mild (desquamation), small loose or partially adherent flakes
3 Moderate (vivid desquamation) large loosely attached flakes with irregular whitish appearance, adherent small white flakes
4 Pronounced (mostly adherent desquamation) large mostly adherent flakes as scarce white or yellow plates
5 Severe (brisk desquamation) adherent flakes as white or yellow plates

Pruiritus/burning and dandruff was to be rated by the patient at baseline, and after 2 and 4 weeks of treatment.

Pruritus/burning score*:*

0 Absent (no pruritus or burning, when asked)
1 Slight (some slight pruritus or burning, when asked, but does not interfere with daily activities or sleep)
2 Mild (pruritus or burning, when asked, but does not interfere with daily activities or sleep)
3 Moderate (pruritus or burning, spontaneously reported, now and then interfering with daily activities or sleep)
4 Pronounced (pruritus or burning, spontaneously reported, interfering regularly with daily activities or sleep)
5 Severe (pruritus or burning, spontaneously reported, interfering extremely with daily activities or sleep)

Dandruff score*:*

0 Absent (no dandruff is noticed)
1 Slight (dandruff is noticed, but not evident without provocation)
2 Mild (some dandruff is noticed)
3 Moderate (visible and evident dandruff)
4 Pronounced (very obvious dandruff)
5 Severe (extreme dandruff)

The Investigator and Patient were to assess treatment efficacy after 4 weeks of treatment as follows:

Investigator's and Patient's global assessment score

0 Fully healed
1 Markedly improved
2 Moderately improved
3 Slightly improved
4 Unchanged
5 Deteriorated

Safety
Safety was to be assessed by recording all directly observed and spontaneously reported adverse events (AEs). Safety was presented using descriptive statistics.

Statistical methods:
Efficacy
The primary efficacy variable was to be analysed with the proportional odds model. Baseline sum scores were to be included in the model as covariates. Secondary efficacy variables were also to be analysed with the proportional odds model, using baseline data as covariates where appropriate. To analyse the secondary efficacy variables complete and partial responders, logistic regression was to be used.

Safety
In the safety analyses, no formal statistical inference was to be performed. Safety variables were to be presented with descriptive statistics.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

Efficacy variable	**Week 2***	**Week 4***
Sum of erythema and desquamation scores	**p=0.0196**	p=0.0783
Erythema score	p=0.4791	p=0.3229
Desquamation score	**p=0.0006**	**p=0.0130**
Investigator's global evaluation	-	**p=0.0115**
Patient's global evaluation	-	**p=0.0087**
Patient's evaluation of pruritus	p=0.0598	p=0.2029
Patient's evaluation of dandruff	p=**0.0436**	p=0.0627
$Responder_0$**	p=0.4187	p=0.1050
$Responder_{0-2}$**	**p=0.0180**	p=0.3150

*Results from the full analysis set (FAS)
**The subscript refers to the sum of erythema and desquamation scores

SAFETY RESULTS:
There were too few events within each system organ class (SOC) category to draw any formal statistical conclusions regarding differences between the treatment groups. While only one out of 7 AEs from the placebo group was judged to be possibly related to the IMP, 18 of 30 AEs from the K301 treatment group were possibly related to the IMP. These were generally application site reactions and the majority were graded as being of mild severity. None of the AEs for either treatment group were graded as "severe" and no SAEs were reported. Furthermore, no patients were withdrawn from the study due to an AE.

CONCLUSION:
Although this study did not attain statistical significance on the primary endpoint, the results for some key secondary efficacy endpoints i.e. the investigator's and patient's global evaluation of treatment effect, desquamation scores at Week 2 and 4 and sum score for erythema and desquamation at Week 2 indicate that K301 has clinically meaningful benefits in the treatment of scalp SE. Finally, the safety results demonstrate that the study product, K301, is generally well tolerated and safe.