1. TITLE PAGE

CONFIDENTIAL

CLINICAL STUDY REPORT

Clinical Study Report Code: M/37779/21

Name of the Investigational product: LAS 37779
Indication studied: Psoriasis
Phase of the study: IIa (proof of principle)

"A DOUBLE-BLIND, RANDOMIZED, PARALLEL, MULTICENTER, VEHICLE-CONTROLLED, LEFT/RIGHT PAIRED COMPARISON TO STUDY THE EFFICACY, SAFETY AND TOLERABILITY OF 1% LAS 37779 CREAM ADMINISTERED ONCE AND TWICE DAILY TOPICALLY DURING 4 WEEKS IN PATIENTS WITH CHRONIC PLAQUE PSORIASIS."
(Protocol No. M/37779/21; Eudract No. 2005-003162-42)

Date of Statistical Report: 21-March-2007
Pharmacokinetic Report No.: B.37779.09
Date of initiation of the study: 14-November-2005
Date of early study termination: Not applicable
Date of completion of the study: 30-April-2006
Date of completion of the Report: 23-Feb-2011

Company / Sponsor:
Almirall, S.A.
Laureà Miró 408-410
08980 Sant Feliu de Llobregat
Barcelona (Spain)
Telephone: +34 93 291 30 00
Fax: +34 93 291 35 33

Principal Investigator:
[redacted]
bioskin GmbH
Poppenbuetteler Bogen 25
22399 Hamburg (Germany)
Telephone: +49-(0)40-606897-0
Fax: +49-(0)40-606 897-30

Clinical Trial Manager:
[redacted]
Laureà Miró 408-410
08980 Sant Feliu de Llobregat
Barcelona (Spain)
Telephone:+34 93 291 39 86
Fax: +34 93 291 35 33

The study was performed in accordance with Good Clinical Practices (GCP) including the archiving of essential documents

2. SYNOPSIS

Name of Sponsor / Company: Almirall, S.A. **Name of Finished Product:** N.A. **Name of Active Ingredients:** LAS 37779	**Individual Study Table Referring to Part of the Dossier** **Volume:** **Page:**	**(For National Authority Use only)**

Title of Study: A DOUBLE-BLIND, RANDOMIZED, PARALLEL, MULTICENTER, VEHICLE-CONTROLLED, LEFT/RIGHT PAIRED COMPARISON TO STUDY THE EFFICACY, SAFETY AND TOLERABILITY OF 1% LAS 37779 CREAM ADMINISTERED ONCE AND TWICE DAILY TOPICALLY DURING 4 WEEKS IN PATIENTS WITH CHRONIC PLAQUE PSORIASIS.

Investigators:

[redacted]

Study centers:
bioskin GmbH, Hamburg, Germany
bioskin GmbH, Berlin, Germany
Dermatologische Praxis Dr. Scholz and Dr. Sebastian, Mahlow, Germany

Publication (reference):
None

Studied period (years):	**Phase of development:** IIa
Date study initiated (first screening): 14-November-2005 Date study finalized (last patient last visit): 30-April-2006	

Objectives:

- To assess the efficacy of 1% LAS 37779 cream once and twice daily during 4 weeks compared to vehicle, in patients with chronic plaque psoriasis.
- To determine the onset of action, the duration of effect and whether rebound was induced in an 8-week single-blind evaluator-blinded follow-up period after stopping the treatment.
- To assess the safety and tolerability of 1% LAS 37779 cream compared to vehicle.
- To investigate the systemic drug and metabolite levels of 1% LAS 37779 cream after single and repeated cutaneous applications in this population of patients.

As an additional and explorative objective, an assessment was made whether or not clinical improvement went along with changes in lesion histomorphology, immunochemistry and gene expression of the psoriatic phenotype.

Methodology:
Prospective, double-blind, randomized, parallel, multicenter, vehicle-controlled, left/right paired intra-patient comparison of repeated cutaneous applications (once and twice a day) of LAS 37779 and vehicle in patients with chronic plaque psoriasis.
Two bilateral symmetrical psoriatic areas of similar size between 20 and 200 cm^2 were selected within each patient. Fifty-two patients were randomized into the trial with a minimum Total Sign Score of 6 in each of the selected areas.
Half of the patients were randomized to receive trial treatments once daily and the other half were randomized to receive treatments twice daily.
For each patient, one selected lesion was randomly assigned to receive 1% LAS 37779 cream and the other one matching vehicle. Patients were instructed to apply the treatment on both selected areas once daily (in the morning) or twice daily (in the morning and evening). Treatment was administered for 28 consecutive days. After completing treatments, a follow-up period of 56 days (8 weeks) after last administration was performed.
A clinical evaluation (Selection Visit), including medical history, laboratory evaluations, vital signs and 12-lead ECG, was performed 1 to 14 days before the first trial drug administration, to confirm the patient's trial eligibility. During the treatment phase, patients were evaluated to assess clinical efficacy on 5 occasions, separated by one-week intervals (Visits 1 –baseline- to Visit 5 –end of the 4^{th} treatment week-). At Visits 1 to 5, the morning medication application was performed at the clinic. (continued)

2. SYNOPSIS

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Methodology (continued):
During the 8-week follow-up period, patients were evaluated to assess the clinical status of the treated areas on 4 occasions separated by two-week intervals (Visits 6 to 9) for up to 8 weeks after stopping treatment.
To investigate the systemic drug levels of LAS 37779 and its main metabolites, blood samples were drawn as follows:
-Group of patients to receive the trial medication once a day (QD regimen):
Visit 1 (Day 1 of treatment [before application and 3h, 6h and 12 hours after application]), Visits 2, 3 and 4 (Days 7, 14 and 21 of treatment [before application]), and Visit 5 (Day 28 of treatment [before application and 3h, 6h, 12h and 24 hours after application]).
- Group of patients to receive the trial medication twice a day (BID regimen):
Visit 1 (Day 1 of treatment [before morning application and 3h, 6h and 12 hours after first application]), Visits 2, 3 and 4 (Days 7, 14 and 21 of treatment [before first application]), and Visit 5 (Day 28 of treatment [before application and 3h, 6h, 12h and 24 hours after application]).
Punch biopsies of lesional areas were taken at Visits 1 (baseline) and 5 (Day 28 of treatment). An additional biopsy of non-lesional skin was collected at Visit 1. Wound healing was controlled at the following Visit after sampling. Photographs of the treated lesions were taken for all patients at Visits 1 and 5.

Number of patients (planned and analyzed):
Planned: Fifty-two patients were to be randomized to ensure at least 40 evaluable patients.

Screened:	72
Randomized:	52
Completed treatment period:	51
Completed follow-up period:	50
Evaluated for efficacy:	48 (PP-population) (QD regimen: 25, BID regimen: 23)
Evaluated for pharmacokinetics:	31 (QD regimen: 16, BID regimen: 15)
Evaluated for pharmacodynamics:	20 (QD regimen: 10, BID regimen: 10)
Evaluated for safety:	52

Diagnosis and main criteria for inclusion:
Males and females aged 18 to 65 with a confirmed clinical diagnosis of stable plaque psoriasis comprising between 3% and 30% of body surface area, provided there are two comparable symmetrical bilateral areas between 20 and 200 cm^2, Total Sign Score (TSS, sum score of erythema, induration and scaling) of at least 6 in each of the selected areas.

Test product , dose and mode of administration, batch number, expiry date:

Name:	LAS 37779
Administration route:	Topical
Dosage form:	1% cream
Dose and regimen:	2 mg/cm^2 once and twice a day, during 28 days.
Batch number:	032F0050 and 033F0051
Expiry date:	03-2006

Duration of treatment:
28 days

Reference therapy, dose and mode of administration, batch number, expiry date:

Name:	Vehicle
Administration route:	Topical
Dosage form:	Vehicle cream
Dose and regimen:	2 mg/cm^2 once and twice a day, during 28 days.
Batch number:	027F0045 and 028F0046
Expiry date:	03-2006

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Criteria for evaluation:

Efficacy:

The efficacy assessment was based on the disease progression of the two lesions identified at baseline. The main efficacy variable was the change from baseline in the Total Sign Score of each treated area at the end of treatment (Day 28). Total Sign Score was defined as the sum of individual scores for erythema, induration and scaling [score 0 (absent) to 4 (very severe) for each sign].

The secondary variables were:

- Change from baseline (Day 1) in the TSS of each treated area to Days 7, 14 and 21 of treatment and Days 14, 28, 42 and 56 after stopping treatment.
- Change from baseline (Day 1) in the score for each of the individual signs (erythema, induration and scaling) of each treated area to Days 7, 14, 21 and 28 of treatment and to Days 14, 28, 42 and 56 after stopping treatment.
- Percentage of treated areas with an Investigator's Global Assessment of Treatment Response rated as ≥50%, ≥75%, ≥90% and 100% clear on Days 7, 14, 21 and 28 of treatment and on Days 14, 28, 42 and 56 after stopping treatment.
  The Investigator's Global Assessment of Treatment Response was assessed by using a 7-point scale: -1=worse; 0=no change; 1=minimal improvement; 2=moderate improvement; 3=marked improvement; 4=almost clear; 5=clear.
- Percentage of treated areas reaching a ≥50% or ≥75% decrease from baseline (Day 1) in Total Sign Score on Days 7, 14, 21 and 28 of treatment and on Days 14, 28, 42 and 56 after stopping treatment.
- Time to reach ≥50% or ≥75% reduction from baseline (Day 1) in Total Sign Score (onset of action).
- Duration of time with ≥50% or ≥75% reduction from baseline (Day 1) in Total Sign Score after stopping treatment (duration of action).
- Percentage of treated areas with an improvement from baseline at Visit 5 (Day 28) of treatment reduced by > 50% in TSS, on Days 14, 28, 42 and 56 after stopping treatment (relapse).
- Percentage of treated areas reaching 125% of baseline (Day 1) Total Sign Score on Days 14, 28, 42 and 56 after stopping treatment (rebound effect).

Pharmacokinetics:

Plasma levels and pharmacokinetic parameters were determined after single (Day 1 of treatment) and repeated application (Day 28 of treatment). On Days 7, 14 and 21 of treatment, plasma drug levels were determined before IMP morning application.

A maximum of thirty-two patients were included for this purpose.

Pharmacodynamics:

Histomorphology, immunochemistry and gene expression:

Changes in these 3 above mentioned items of punch biopsies of treated lesional areas taken at baseline and Day 28 of treatment.

- Histological phenotype, epidermal thickness, quality and quantity of the inflammatory infiltrate, architecture of the papillary blood vessels, papillomatosis, perifocal and epidermal reactions.
- Qualitative description of the inflammatory cell infiltrate, reactions with different monoclonal antibodies directed to antigens CD1a, CD3, CD4, CD8, CD25, CD31, CD35, CD54, HLA-DR, filaggrin, involucrin, keratin-16, Ki-67, CD11c and CD83.
- RNA analysis: K16, ICAM-1, IFN-γ, IL-2, IL-7R, IL-7, IL-8, IL-12(p40), IL-23(p19), IL-12(p35), IL-15, IL-17, IL-19, IL-20, TNF-α, STAT-1, STAT-3, TRIM22, IP-10, IRF-1, RANTES, CTLA-4, IL-10, IKBα, MIG, S100A9, ID4, GADPH.

For this purpose punch biopsies were obtained from a maximum of twenty patients. (continued)

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Criteria for evaluation (continued):

Safety and tolerability:

Adverse events recorded during the treatment and follow-up phases, including laboratory evaluations, vital signs and 12-lead ECG and Global Assessment of Tolerability.

Other variables:

Number of withdrawals and reasons for withdrawal.

Statistical methods:

The same statistical analyses were performed for both treatment regimens and those were performed independently from each other, this is, there were analyses comparing LAS 37779 1% cream qd and vehicle qd and separately the same statistical analyses were produced comparing LAS 37779 1% cream bid and vehicle bid.

In all statistical tests, the significance level (probability of Type-I error) was set at 0.05 two-tailed.

All efficacy data are listed.

Main variable:

The analyses of the primary efficacy variable were performed on the PP population.

For each treatment (LAS 37779 1% cream qd/bid and Vehicle qd/bid), raw values and changes from baseline (Day 1) in TSS of each treated area to the end of treatment (Day 28) were summarized by means of descriptive statistics.

The treatment comparisons were:

LAS 37779 1% cream qd versus Vehicle qd

LAS 37779 1% cream bid versus Vehicle bid

The comparison between treatments (LAS 37779 1% cream qd/bid and vehicle qd/bid) of the change from baseline (Day 1) in the TSS after 28 days of treatment were carried out using the Wilcoxon signed rank test. The median statistic of the differences were estimated using the Hodges-Lehmann estimator for paired samples.

Secondary variables:

All secondary efficacy analyses were performed on the Per Protocol population (PP).

Secondary efficacy variables are presented using descriptive summaries. The following variables:

- Change from baseline in the TSS of each treated area on Days 7, 14, and 21 of treatment.
- Change from baseline in the score for each of the individual signs (erythema, induration and scaling) of each treated area on Days 7, 14, 21 and 28 of treatment and on Days 14, 28, 42 and 56 after stopping treatment.

were analyzed using the same statistical approach as for the main variable.

For the following secondary efficacy variable:

- Percentage of treated areas with an Investigator's Global Assessment of Treatment Response rated as (≥50% vs. <50%), (≥75% vs. <75%), (≥90% vs. < 90%) and (100% vs. <100%) clear on Days 7, 14, 21 and 28 of treatment and on Days 14, 28, 42 and 56 after stopping treatment.

descriptive statistics for categorical data were produced by visit and treatment group. Also, it was analyzed by means of the McNemar test for paired data (2*2 contingency tables) in order to detect differences by treatment groups.

For the following secondary efficacy variables:

- Percentage of treated areas reaching a ≥50% or ≥75% decrease from baseline (Day 1) in Total Sign Score on Days 7, 14, 21 and 28 of treatment and on Days 14, 28, 42 and 56 after stopping treatment.
- Percentage of treated areas with an improvement from baseline at Visit 5 (Day 28) of treatment reduced by > 50% in TSS, on Days 14, 28, 42 and 56 after stopping treatment (relapse).
- Percentage of treated areas reaching 125% of baseline (Day 1) Total Sign Score at 14, 28, 42 and 56 after stopping treatment (rebound effect).

descriptive statistics for categorical data were produced by visit and treatment group. (continued)

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Statistical methods

Secondary variables (continued):

For the following secondary efficacy variables:

- Time to reach ≥50% reduction from baseline (Day 1) in Total Sign Score (onset of action).
- Time to reach ≥75% reduction from baseline (Day 1) in Total Sign Score (onset of action).
- Duration of time with ≥50% or ≥75% reduction from baseline (Day 1) in Total Sign Score after stopping treatment (duration of action).

descriptive statistics for continuous data were produced by visit and treatment group.

Safety outcomes:

All safety analyses were performed on the Safety population.

Appropriate descriptive analyses were performed for the following safety outcomes:

Adverse Events (AEs), Physical examinations, Vital signs, Clinical laboratory evaluations (haematology, biochemistry, urinalysis and coagulation)and ECG (12-leads).

Global assessment of tolerability

Descriptive statistics were produced for the global assessment of tolerability presenting the number and percentage of patients falling in the categories “Poor”, “Fair” and “Good” of each treated area at Visit 5 (Day 28) of treatment and Visit 9 (Day 56) after stopping treatment.

Global Assessment of Tolerability between treatments (LAS 37779 1% cream qd/bid and Vehicle qd/bid) were analyzed using the Wilcoxon Rank Sign test. The median statistic of the differences were estimated using the Hodges-Lehmann estimator for paired samples.

Pharmacokinetic parameters:

All PK analyses were performed on the Safety population.

Full descriptive statistics were given for all pharmacokinetics parameters.

Other variables:

All number of withdrawals and biopsy results were summarized on the Safety population.

Full descriptive statistics were given for these parameters. Appropriate tests depending on the nature of the biopsy variables were performed.

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RESULTS

Efficacy Results

The study preparation with LAS 37779 1 % demonstrated a moderate antipsoriatic effect in this paired comparison, vehicle-controlled study with once (QD regimen) and twice daily (BID regimen) treatment over a 28-day period in patients with moderate to severe chronic plaque-type psoriasis. Compared to the active-ingredient free vehicle LAS 37779 1 % improved the Total Sum Score (TSS) significantly from the third week of treatment with once daily application and from the second week with twice daily application.

A significant improvement compared to the vehicle was also seen for the individual scores erythema and induration, but only for the BID regimen. Erythema had significantly improved from the third week of treatment and induration after four weeks. No significant differences compared to the vehicle were noted for scaling in any of the patients during the treatment phase.

After four weeks of treatment with LAS 37779 1 % a percent decrease from baseline in TSS $\geq$ 50 % was noted in 8 of 25 patients following once daily application and in 12 of 23 patients following twice daily application. Two patients of the BID regimen demonstrated reductions in TSS $\geq$ 75 %. A percent reduction in TSS $\geq$ 50 % was also seen in the area treated with the vehicle on Day 28 but in less patients (QD: 4 of 25 patients; BID: 6 of 25 patients). In both regimens one patient demonstrated a reduction in TSS $\geq$ 75 % following treatment with the vehicle. Over the entire study (including follow-up period) some more patients achieved a reduction in TSS $\geq$ 50 % (QD: 12 of 25 patients; BID: 13 of 23 patients) following treatment with LAS 37779 1 %. The time to achieve this reduction ranged between 7 and 71 days for the QD regimen and between 8 and 85 days for the BID regimen. Following treatment with the vehicle there was one more patient in both regimens who achieved a reduction in TSS $\geq$ 50 % (QD: 5 of 25 patients; BID: 7 of 23 patients) regarding the entire study period including follow-up phase. The time to achieve this reduction ranged between 15 and 44 days for the QD regimen and between 15 and 57 days for the BID regimen.

During the follow-up phase the TSS and the individual scores remained clearly lower in most of the patients (QD and BID regimens) following treatment with LAS 37779 1 % and the vehicle. The majority of the patients demonstrated no relapse. For the duration of time with a reduction in TSS $\geq$ 50 % after treatment stop a median of six weeks was noted for LAS 37779 1 % in both regimens. For the vehicle the median was two weeks in the QD regimen and eight weeks in the BID regimen.

The moderate efficacy was also reflected by the improvement of the Investigator's Global Assessment of Treatment Response Score. Compared to the vehicle LAS 37779 1 % improved the Investigator's Global Assessment of Treatment Response Score significantly over a 28-day period with once and twice daily application. A significant improvement was already seen after three weeks treatment in the patients with the BID regimen.

An at least moderate improvement ($\geq$ 50 % clear) was noted in 11 of 25 patients after four weeks of treatment with LAS 37779 1 % once daily and in 14 of 23 patients following twice daily application. Nevertheless, an at least marked improvement ($\geq$ 75 % clear) was only seen in one patient of the QD- and in three patients of the BID regimen. A complete resolution was not reached in any of the patients. An improvement of the Investigator's Global Assessment of Treatment Response Score was also seen for the vehicle on Day 28, however less patients demonstrated an at least moderate improvement (QD: 4 of 25 patients; BID: 7 of 23), with one patient in each regimen demonstrating an at least marked improvement.

Overall, the study preparation with LAS 37779 1 % and the vehicle were well tolerated. Worsening of psoriasis only occurred in one patient of the QD regimen in areas treated with both, LAS 37779 1 % and the vehicle. No worsening was noted for patients of the BID regimen. In none of the patients a rebound effect (125 % of baseline TSS) was noted at any test point during the follow-up period, neither for LAS 37779 1 % nor for the vehicle following once or twice daily application.

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RESULTS (continued)

Pharmacokinetic Results:

The plasma levels of LAS 37779 and its metabolites LAS 39163, LAS 38914 and LAS 100090 found in this clinical trial confirm the percutaneous absorption of LAS 37779 from the 1% LAS 37779 cream in psoriasis patients. Following once- or twice-daily application of 1% LAS 37779 cream, the main metabolite circulating in plasma was LAS 100090, achieving concentrations in general about 2-fold higher than those of the parent drug, whereas the metabolite LAS 38914 was found at lower plasma concentrations. The plasma levels of the metabolite LAS 39163 were very low (close to LLOQ when measured) whereas the metabolite LAS 39034 and the additional metabolite LAS 100744 were not detected in any of the samples analysed. The rank order of the plasma levels of LAS 37779 and its metabolites obtained after the once or twice-daily application of the 1 % LAS 37779 cream was:

LAS 100090 > LAS 37779 > LAS 38914 >> LAS 39163; (LAS 39034 and LAS 100744 were not detected).

The low plasma concentrations observed for LAS 37779 after the first application (day 1) in comparison to those found on day 28 indicated a slow rate of absorption after a single cream application. This finding was in agreement with the results found in the previous phase I clinical trial after single and repeated ascending cutaneous application of LAS 37779 to healthy male subjects. These results also suggest that there is an improvement of the rate of skin penetration due to the repeated cream application. The Cmax, Cmin and AUC values found for LAS 37779 and its metabolites after the twice-daily cream application were higher than those obtained after the once-daily application. However, due to the high variability found in the calculated pharmacokinetic parameters together with the reported variations in the amounts of cream applied between patients, no clear dose proportionality was found. The mean maximum plasma concentration for LAS 37779 at steady state ($Cmax^{ss}$, day 28) was 0.398 $\pm$ 0.271 and 0.698 $\pm$ 0.734 ng/ml for the once- and twice-daily treatments, respectively. The time to reach the $Cmax^{ss}$ (tmax) was approximately 10 h for both treatments. The mean AUC (0-12) values were 2.55 $\pm$ 1.68 ng.h/ml for the once-daily treatment and 3.98 $\pm$ 4.21 ng.h/ml for twice-daily treatment (the latest value corresponds to $AUC\tau^{ss}$, τ=12h). Considering that on day 28 of treatment only one cream application was performed in the morning in the two dose regimens studied, the mean AUC (0-24) values found were 4.78 $\pm$3.46 ng.h/ml for the once-daily dose regimen and 7.71 $\pm$ 7.07 ng.h/ml for the twice-daily dose regimen. Taking into account the limited number of kinetic time-points included in the study and the different potential sources of variation in the dose absorbed (differences in the amount of cream consumed by each patient, improvement of the skin condition throughout the treatment period, age differences in the skin lipid content, anatomical sites, etc) the exposure, regarding pharmacokinetic parameters obtained in the present study, should be considered as exploratory when comparing study treatments or with other studies in healthy volunteers or patients with chronic plaque psoriasis.

Pharmacodynamic Results:

Overall, the results of the histomorphology and immunochemistry assessments did not reflect the moderate antipsoriatic effect seen in the efficacy analyses. In the histological assessment no significant reduction in inflammatory infiltrate was seen after treatment with LAS 37779 1 % as compared with the active-ingredient free vehicle and no differences were noted in the density of inflammatory cells.

The immunohistochemical analyses showed no significant differences between LAS 37779 1 % and the vehicle. No relevant changes in the proportion of inflammatory cells were observed neither after four weeks of treatment with LAS 37779 1 % nor the vehicle.

The assessment of gene expression showed statistically significant differences between non-lesional skin and lesions for most genes. However, significant differences in gene expression between untreated lesions and lesions treated with LAS37779 were only seen for Keratin 16, IL8, IL19, Elafin, IL-23(p19) and ID4, whereas statistically significant differences were also found following treatment with the vehicle for Keratin 16, IL8 and IL-23(p19).

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RESULTS (continued)

Safety and Tolerability Results:

No safety and tolerability concern is evidenced in this study with regard to LAS 37779 1 % based on AE reported during the study or any of the other safety evaluations performed throughout the study.

None of the AEs were considered related to LAS 37779 1 % or the vehicle and the dermal tolerance was very good. During the follow-up period one local AE in one patient (QD regimen) was noted for both LAS 37779 1 % and the vehicle. A postoperative wound infection following biopsies was noted for this patient in both treatment areas. The patient used a concomitant medication due to this AE.

In the laboratory examinations clinical relevant abnormal findings were noted in the biochemistry analyses:

In the QD regimen relevant abnormal triglyceride values were noted for four patients and a relevant abnormal gamma GT value in one patient after four weeks of treatment. No medication was taken, but the values were controlled. Eight weeks after treatment stop the increased blood triglycerides had turned to normal in one patient and were assessed as not clinical relevant in another patient. In two patients the blood triglycerides were still increased at the control after study end and the patients were sent to a practitioner. The gamma-glutamyltranferase was assessed as not clinical relevant at the last visit.

In the BID regimen relevant abnormal triglyceride values were noted in two patients and a relevant abnormal glucose value in one patient after four weeks of treatment. No medication was taken, but the values were controlled and assessed as not clinical relevant. Eight weeks after treatment stop relevant abnormal triglyceride values were noted again in one of the two patients and also in another patient. In case of both patients the values were still clinical relevant after the control and the patients were sent to a practitioner. In addition an abnormal creatine kinase value with clinical relevance was noted in one patient at the last study visit. This value was to be controlled by practitioner.

None of these abnormal laboratory findings was considered to be related to the study medication.

No relevant abnormalities were found in the physical examination and vital signs or ECG evaluations.

In the global assessments of tolerability both treatments LAS 37779 1 % and the vehicle were rated as “good” in all patients in both regimens.

CONCLUSIONS:

In this study it was found that LAS 37779 1 % led to a moderate improvement of the psoriatic plaques. Compared with its vehicle LAS 37779 1 % showed a significant effect from the third week of treatment with once daily application and from the second week with twice daily application. The moderate efficacy was reflected in the TSS, the individual clinical assessment scores and in the Investigator’s Global Assessment of Treatment Response score. However, the difference between LAS 37779 1 % and its vehicle could not be confirmed histologically. No relevant reduction of the thickness of the psoriatic infiltrate and no reduction of the density of cells of the psoriatic infiltrate were noted.

The plasma levels of LAS 37779 and its metabolites LAS 39163, LAS 38914 and LAS 100090 found in this clinical trial confirm the percutaneous absorption of LAS 37779 from the 1 % LAS 37779 cream in psoriasis patients. The RNA analysis showed no relevant change in gene expression following treatment with LAS 37779 1 %.

Overall, LAS 37779 1 % demonstrated moderate antipsoriatic efficacy in the treatment of moderate to severe psoriasis vulgaris while being safe and well tolerated. No safety and tolerability concern is evidenced in this study with regard to LAS 37779 1 % based on AE reported during the trial or any of the other safety evaluations performed throughout it.

DATE OF REPORT: 23-02-2011