Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

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## Clinical Trial Results Synopsis

### Study Design Description

| Study Sponsor: | Bayer Healthcare AG |
| Study Number: | 87105 | NCT00000000 |
| Study Phase: | III |
| Official Study Title: | Controlled, double-blind group comparison of a twice daily (maximum 3 weeks) use of methylprednisolone aceponate 0.1 % cream and prednicarbate 0.25 % cream (Dermatop) in children with atopic dermatitis |
| Therapeutic Area: | Dermatology |

#### Test Product

| Name of Test Product: | Advantan 0.1% cream (Methylprednisolone Aceponate, BAY86-4862) |
| Name of Active Ingredient: | Methylprednisolone Aceponate |
| Dose and Mode of Administration: | Twice daily topical application for a maximum of 3 weeks applied to skin either openly or under dressing or under occlusion |

#### Reference Therapy/Placebo

| Reference Therapy: | Prednicarbate 0.25 % cream (Dermatop) |
| Dose and Mode of Administration: | Twice daily topical application for a maximum of 3 weeks applied to skin either openly or under dressing or under occlusion |

#### Duration of Treatment:

The duration of treatment was limited to a maximum of 3 weeks. The treatment was concluded as soon as the doctor had assessed the lesions to be healed.

#### Studied period:

| Date of first subjects’ first visit: | October 1987 |
| Date of last subjects’ last visit: | May 1988 |

#### Study Center(s):

8 dermatologists in private practice treated patients in one country: Federal Republic of Germany

#### Methodology:

The study was conducted to evaluate the therapeutic efficacy and tolerance of methylprednisolone aceponate 0.1 % cream and prednicarbate 0.25 % cream (Dermatop) in 80 children (40 per group) on an out-patient treatment in a controlled, randomized, double-blind, multicentre, group comparison design. Twice daily application was specified for a maximum period of three weeks. The treatment was concluded as soon as the doctor had assessed the lesions to be healed. The treatment was to be discontinued if the therapy was ineffective or if the pathological skin changes deteriorated or if severe corticoid-induced local and/or systemic concomitant symptoms occurred. Four examinations were performed to assess the course of the therapy on days 3-5, 6-8, 9-14 (week 2) and 15-21 (week 3). Development of the objective symptoms and subjective symptoms was to be assessed and documented by the attending doctor according to the following categories: severe = 3, mild = 2, absent =
| Indication/ Main Inclusion Criteria: | Children of both sexes between the ages of three and 14 years suffering from a mild or moderately severe atopic dermatitis were included in study. The legal guardian of each child had to give her/his consent to the participation of her/his child in the study before the start of treatment. |
| Study Objectives: | **Overall:** The aim of this multicentre study was to compare the therapeutic efficacy and tolerance of methylprednisolone aceponate 0.1 % cream after a twice daily and a maximum of 3 weeks' use in a double-blind group comparison with prednicarbate 0.25 % cream (Dermatop) in children with atopic dermatitis.  
**Primary:** Not applicable  
**Secondary:** Not applicable |
| Evaluation Criteria: | **Efficacy (Primary):** The main criterion for the evaluation of efficacy was the assessment of the therapeutic effect by the investigator.  
**Efficacy (Secondary):** An "objective score" was calculated as sum of all assessments of objective symptoms (erythema, rhagades, scaling, prurigo, excoriation and lichenification) and a "subjective score" was calculated as sum of evaluations of subjective symptoms (itching and pain).  
**Safety:** The local and general tolerance of was compared between test and reference. Any local or general concomitant symptoms at the time of the assessments of the therapy were recorded. |
| Statistical Methods: | **Efficacy (Primary) - if applicable:** A cure rate ("complete healing") of about 70% was assumed for the comparative treatment. Considering probabilities of $\alpha = 0.05$ and $\beta = 0.10$ for the type I and type II errors, "Fisher's exact method" was used to discern a difference of 25% between the rates for "complete healing" under therapy with test and reference.  
**Efficacy (Secondary) - if applicable:** Seconary criteria for the comparison of the therapies were the scores for objective and subjective symptoms. These comparisons were based on Mann-Whitney-U-test with $\alpha = 0.05$. Global comparisons frequency tables were given for each objective and subjective symptoms per point of time. "Fisher's exact method" was performed without an adjustment of error probabilities with respect to the number of variables and points of time.  
**Safety:** The numbers of local concomitant symptoms of the two treatment groups were compared (Fisher-test, $\alpha = 0.05$). |
Number of Subjects: It was planned to randomize 80 patients with 40 in each treatment arm. Out of 79 patients randomized, 39 received test therapy and 40 received reference therapy. Out of the 79 patients, one subject was not included in the evaluation after the end of the study because of non-adherence to the exclusion criteria (systemic corticoid in the last 4 weeks before start of study) and a total of 78 patients were evaluated.

Study Results

Results Summary — Subject Disposition and Baseline

A total of 78 patients were evaluated in the study, with 40 patients in Dermatop arm and 38 in methylprednisolone aceponate arm. Forty (51.3%) were male (median age 8 years) and 38 (48.7%) were female (median age 8.5 years). There was no difference between the treatment groups with regard to age and gender distribution.

The study preparations were used mainly on the arms, legs and trunk in 73.1% patients which corresponded to the sites with predilection of the disease. In the majority of the patients (test 92.1%, Dermatop 87.5%) the type of skin was assessed as "dry". Most of the cases were assessed as moderately severe (almost 80% in each group); 13.2% cases in test were assessed as severe as compared to 7.5% cases in Dermatop. The disease was chronic or recurrent in most of the cases (test 71.1% and Dermatop 80%).

The duration of the disease ranged from 2 weeks to 13.7 years (median 2.9 years), and the median of the existing time of the disease was 3.9 years in the test and 2.9 years in the Dermatop group. Erythema, scaling and itching were the symptoms most frequently diagnosed by the investigator or reported by the patients.

Almost 47.4% (test) and 40% (Dermatop) subjects had received previous treatment with topical corticoid. All 40 patients receiving Dermatop therapy completed study while 36 out of 38 patients in test arm (94.7%) completed the study as scheduled. I patient was lost to follow-up and 1 patient had early treatment success in week 2.

Results Summary — Efficacy

The statistical analysis of the baseline values of the cumulative scores (objective symptoms) showed significant differences (α = 0.05) between the test and reference therapy with test arm showing more severe cases and also higher number of subjects suffering from individual symptoms.

At the end of the study at the point of last assessment, the objective and subjective symptoms regressed nearly completely and almost equally well in both treatment groups. Depending on the symptom 66% to 100% of the patients were symptom-free at the end of therapy.

As per final assessments of the therapeutic effect by the investigator, 26 patients (68.4%) of the MPA arm and 30 patients (75%) of the Dermatop arm were assessed as "completely healed" and 11 (29%) from MPA arm and 10 (25%) from Dermatop as "distinctly improved". Thus there was total therapeutic success of 97.4% in MPA arm as compared to 100% in Dermatop arm, which was not a significant difference between the two treatment groups.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Complete healing (%)</th>
<th>Distinct improvement (%)</th>
<th>Moderate effect (%)</th>
<th>No effect (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantan 0.1% cream</td>
<td>26 (68.42%)</td>
<td>11 (28.95%)</td>
<td>1 (2.63%)</td>
<td>0 (0%)</td>
<td>38 (100%)</td>
</tr>
<tr>
<td>Dermatop 0.25% cream</td>
<td>30 (75%)</td>
<td>10 (25%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>40 (100%)</td>
</tr>
</tbody>
</table>
As expected the lichenification was the symptom with the fewest "symptom-free" patients at the end of therapy in both test (56%) and reference (70.8%). The number of patients, in whom some of the symptoms were assessed as "unchanged" at the end of therapy (especially lichenification) was nearly the same in both treatment groups. Altogether the therapeutic results for all symptoms were equally good in both treatment groups. There was no significant difference at any of the time-points (α = 0.05) between the investigational and reference preparation by using the Fisher-test for subjective as well as objective symptoms.

With regards to the different degrees of severity present at the start of the study, as well as the different disease states (acute/chronic/recurrent) both preparations proved themselves to be therapeutically equally effective.

Results Summary — Safety

Local concomitant symptoms were mentioned by 5 out of 38 children receiving MPA and 3 out of 40 children receiving Dermatop. In all of these 8 patients only a mild burning was mentioned in the first or second week under dermal open use. No accompanying measures by the investigator due to the complaints were necessary. Typical corticoid concomitant symptoms like atrophy, telangiectasia, etc. did not occur in either arms.

Conclusion(s)

In this group comparison study good therapeutic results were achieved with both preparations.

Although the baseline severity scores were not the same for both treatment groups with more severe objective symptoms in the test group, no differences were found between the two preparations, either with regard to the regression of the symptoms or the assessments of the therapeutic effect at any time.

The tolerance of both preparations was good and only local concomitant symptoms (in all cases mild burning) were diagnosed in all cases, likely reason for which was type of base, i.e. the low fat content of the teo cream preparations. Typical symptoms related to corticosteroids were not observed in either group.

In summary, in this study there were no differences between methylprednisolone aceponate 0.1 % cream and the reference preparation (Dermatop 0.25 % cream) with respect to either the therapeutic efficacy or the tolerance.