Clinical Efficacy and Tolerability of a Novel Selective Corticosteroid in Atopic Dermatitis – Two Randomised Controlled Trials

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Key Words
Atopic dermatitis · Corticosteroids · Treatment · Atrophy

Abstract
Topical corticosteroids remain the first-line therapy for atopic dermatitis (AD). Hence, we investigated the efficacy and safety profile of a novel selective corticosteroid, GW870086. We performed 2 randomised, double-blind, controlled studies with 25 AD patients and 20 healthy subjects. The changes in the Three-Item Severity (TIS) score and the skin thickness were the primary end points, respectively. The adjusted TIS score (day 22) shows that the novel corticosteroid resulted in a non-significant, but dose-dependent reduction compared to placebo (GW870086 0.2% vs. placebo = −0.38, GW870086 2% vs. placebo = −0.89). Significant skin thinning was observed in the second study on days 14 and 21 when patients were treated with the comparator but not with the novel corticosteroid compared to placebo. The clinical efficacy of the new selective corticosteroid was not superior to placebo, although a dose-dependent improvement upon treatment was noticed without the onset of skin thinning.

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease which requires long-term management. Hitherto, despite the introduction of topical calcineurin inhibitors acting selectively on T cells, topical corticosteroids remain the first-line therapy for AD [1]. However, the therapeutic anti-inflammatory efficacy of topical corticosteroid treatment can be associated with the onset of local side effects such as the development of telangiectasia and skin thinning [2]. These side effects can occur particularly if corticosteroids are used for long periods of time without interruption.

On a mechanistic level, the therapeutic effects of corticosteroids are mediated by a negative regulation of inflammatory gene expression (transrepression) [3]. Their unwarranted side effects are believed to be mediated by a direct induction of gene transcription (transactivation) [4]. Therefore, the development of novel corticosteroids for AD treatment focuses on the introduction of selective corticosteroids which display a reduced side effect profile while maintaining their anti-inflammatory and immunosuppressive properties [4].
We conducted 2 clinical studies to investigate the efficacy and safety profile of a new selective corticosteroid, GW870086, currently under development for AD in children. GW870086 has been demonstrated to have potent corticosteroid effects in several in vitro and in vivo models [5–7]. Its selectivity has been proven by its ability to enable the glucocorticoid receptor to transpress, but the molecule itself has little effect on transactivation (online suppl. fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000367696) [5]. This novel corticosteroid also shows superior selectivity for the glucocorticoid receptor over the progesterone and mineralocorticoid receptors compared to other corticosteroids. Thus, it may provide a beneficial topical treatment for AD with a reduced side effect profile.

In our study, we first evaluated the clinical efficacy and tolerability of GW870086 at 2 different concentrations in AD patients in comparison to placebo. Fluticasone propionate (FP) served as a positive comparator. Secondly, we assessed the skin-thinning potential of GW870086 in comparison to clobetasol propionate (CP) by measuring the skin thickness of treated lesions in healthy subjects with ultrasound.

Methods

Both studies were set up in 2011 and were carried out in the same year as randomised, double-blind, placebo-controlled clinical trials. The trial protocols were approved by the ethics committee of Berlin and by the responsible authority. The participants were recruited at the Allergy-Centre-Charité, and written informed consent was obtained from each participant. Both studies were registered at the GSK Clinical Study Register and at Clinical-Trials.gov (NCT0129961, NCT00549497).

Two cohorts were enrolled (online suppl. table 1): (1) patients suffering from moderate to severe AD (study A) and (2) healthy control subjects (study B).

Clinical Efficacy (Study A)

Participants

Patients (18–65 years old) with a diagnosis of AD were included. AD was defined as a documented history of AD as defined by Hanifin and Rajka and modified by Williams et al. [8]. A score of >25 points using the modified Severity Scoring of Atopic Dermatitis rating scale and a body surface area involvement of >5% as assessed by the rule of nines method were required for inclusion in the study. Additionally, the patients had 3 comparable index lesions (≥1 cm² in size) with a sum score of ≥4 and ≤6 for erythema, oedema/papulation and excoriation using the Three-Item Severity (TIS) score [9]. The lesions represented common lesions, i.e. not the most or least severe lesions.

The main exclusion criteria were the presence of any other systemic disorder or active skin disease that could in any way confound the interpretation of the study results. Patients were not allowed to receive any other local treatments (e.g. with tar, corticosteroids (except topical 1% hydrocortisone) or retinoids) within 14 days prior to the first application of the study drug. Systemic treatments for AD within 28 days of the first dose of study drug were prohibited.

Treatment

Patients were randomly assigned to receive 3 out of 4 treatments: placebo cream, GW870086 0.2% cream, GW870086 2% cream and FP 0.05% cream. Three target lesions were located on the arms and/or legs and/or torso and/or neck. In all patients, 1 assigned treatment was placebo. Each treatment was applied to the same lesion once daily throughout 21 ± 2 days. On days 1–3, patients were shown by trained site staff how to apply the cream. The patients applied their study treatments under supervision also on days 7 ± 2, 14 ± 2 and 21 ± 2. On all the other days, treatments were applied at home.

TIS Score

The primary end point of study A was the change from baseline in the TIS score on day 22 (24 h after the last dose). The effect was compared between GW870086 0.2% and 2% relative to placebo. The TIS score is the sum of 3 intensity items (erythema, oedema/papulation, excoriation) scored on a 4-point scale from 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe) with a maximum of 9 points.

Immunohistochemistry

In a subgroup of AD patients, biopsies from each treated lesion were used to detect changes in skin thickness and for exploratory biomarker analysis. Before and after treatment (day 1 and day 22), a 4-mm punch skin biopsy was taken from each of the 3 target lesions. Samples of formalin-fixed, paraffin-embedded skin biopsies were analysed as described previously [10]. Images were acquired using an Axiolab Z1 microscope (Carl Zeiss Micro-Imaging Inc., Jena, Germany). CD4+ and CD8+ cells were quantified per high-power field (0.237 mm²), and 5 high-power fields were averaged in each case. Proliferating Ki-67+ cells were quantified per 100 basal keratinocytes, and carboxyterminal propeptide of type I procollagen (PICP) was semi-quantified. All immunohistochemical evaluations were performed in a blinded manner. A mean baseline subject level was calculated for statistical analyses, which were performed with non-parametrical tests, either the Wilcoxon test for paired data (before and after treatment) or the Kruskal-Wallis/Mann-Whitney U test for unpaired data (treatment group comparison). SPSS statistics (SPSS Inc., Chicago, Ill., USA) was used, and the data were expressed as medians with ranges.

Skin Thinning (Study B)

Participants

Healthy subjects between 18 and 55 years of age were included. Three areas of approximately 5 × 5 cm on the arm were identified, and each treatment was applied once daily to the same area throughout the treatment period of 42 ± 2 days.
Subjects who received CP 0.05% applied this once daily for a maximum of 21 ± 2 days (in an open manner as a positive control) and continued with the 2 other treatments in a blinded manner. On days 1–3, the subjects were shown by trained site staff how to apply the cream. The subjects applied their study drugs under supervision once a week (on days 7 ± 2, 14 ± 2, 21 ± 2, 28 ± 2, 35 ± 2 and 41 ± 2). On all the other days, the study drugs were applied at home.

Skin Thinning
The primary end point was the change in skin thickness from baseline between GW870086 (0.2% and 2%) and placebo, measured with ultrasound. If significant evidence of skin thinning (25% reduction in skin thickness) was observed in any of the treatment arms, the application of that treatment was discontinued. Each of the 3 selected areas was assessed for total skin thickness using an ultrasound machine (SkinScanner DUB, tmp, Lüneburg, Germany) with a 2-dimensional configuration device. An expert investigator, who was completely blinded to the treatment allocation of the subjects, performed and recorded the ultrasound assessments. The measurements were performed at each visit prior to the application of the study drug. Additionally, skin thinning was assessed by the investigator using a visual scoring system (a 5-point scale from 0 = none to 4 = very severe) for skin atrophy and telangiectasia.

Randomisation, Sample Size and Statistical Analysis

Study A
25 AD patients were assigned to receive 3 out of the 4 treatments in a double-blind 3-period incomplete block crossover design. The randomisation schedule was generated by Discovery Biometrics (GSK-validated internal software) prior to the start of the study. All 25 AD patients were randomised to receive placebo, with 20 randomised to GW870086 0.2%, 15 randomised to GW870086 2% and 15 randomised to FP 0.05%. The sample size of 25 was chosen based on feasibility, to allow an evaluation of the changes from baseline in the skin thickness of healthy adult volunteers, measured with ultrasound. An expert investigator, who was completely blinded to the treatment, measured the epidermal thickness and the extent of skin thinning in the amount of time over which each dose is administered and each point in time as being ≤1, irrespective of the baseline value of the lesion.

Analysis
The change from baseline in the TIS score between GW870086 and placebo, was analysed by mixed effects model repeated measures (MMRM) analysis, with the primary inference being the difference between GW870086 (0.2 and 2%) and placebo. The change in skin thickness of healthy adult volunteers, measured with ultrasound. If significant evidence of skin thinning (25% reduction in skin thickness) was observed in any of the treatment arms, the application of that treatment was discontinued. Each of the 3 selected areas was assessed for total skin thickness using an ultrasound machine (SkinScanner DUB, tmp, Lüneburg, Germany) with a 2-dimensional configuration device. An expert investigator, who was completely blinded to the treatment allocation of the subjects, performed and recorded the ultrasound assessments. The measurements were performed at each visit prior to the application of the study drug. Additionally, skin thinning was assessed by the investigator using a visual scoring system (a 5-point scale from 0 = none to 4 = very severe) for skin atrophy and telangiectasia.

Study B
20 subjects were assigned to receive 3 out of the 4 treatments in a double-blind 3-period incomplete block crossover design. The randomisation schedule was generated by Discovery Biometrics (GSK-validated internal software) prior to the start of the study. All 20 subjects were randomised to receive placebo and GW870086 2%, with 15 randomised to GW870086 0.2% and 5 randomised to CP 0.05%. The sample size of 20 patients was chosen based on feasibility, to allow an evaluation of the changes from baseline in the skin thickness of healthy adult volunteers, measured with ultrasound.

Analysis
The change in the thickness of the skin layers from baseline was analysed by MMRM analysis as described above, and the difference between both doses of GW870086 and placebo on day 42. The CP comparison was performed in a model separate from that which compared both doses of GW870086, due to the differences in the amount of time over which each dose is administered and data collected.

Results
Clinical Efficacy and Tolerability of the Novel Corticosteroid in AD Patients (Study A)
First, we assessed the clinical efficacy in single lesions via the TIS score by using 2 different concentrations of the novel corticosteroid in comparison to placebo and FP, a mid-strength corticosteroid, as a positive control (fig. 1).

The percentage of responders in the placebo group was 32% (8 of 25), with the responder rates in the GW870086 0.02% and GW870086 2% groups being comparable but only marginally higher than in the placebo group (35% and 40%, respectively). FP 0.05% had the highest response rate, namely 73% (11 of 15, table 1).

The results of the TIS scores of study A on day 22 show that the novel corticosteroid on average displayed a reduction of the TIS scores in both doses relative to placebo (GW870086 0.2% vs. placebo = –0.38, 95% CI –1.46 to 0.70; GW870086 2% vs. placebo = –0.89, 95% CI –2.00 to 0.23). However, the improvement of the TIS scores did not reach significance compared to placebo. By contrast, FP 0.05% versus placebo (–1.51, 95% CI –2.65 to –0.36) displayed a clear and significant reduction of the TIS score (fig. 2).

To assess the atrophogenic potential of the corticosteroid, we measured the epidermal thickness and the expression of procollagen from lesional skin before and af-
To get more insights into the clinical efficacy, we performed immunohistochemical analyses of exploratory biomarkers, such as the proliferation marker Ki-67, and of the frequency of CD4+ and CD8+ T cells in skin biopsies from lesional skin.

The data show no change in epidermal thickness (fig. 3a) before and after placebo treatment. By contrast, FP 0.05%-treated lesions exhibited a significant decrease in epidermal thickness after the 3-week treatment course \( (p = 0.018) \) and in comparison to placebo \( (p = 0.007) \), which was accompanied by a reduced individual cell size (online suppl. fig. 2). In the GW870086-treated groups, although this was not statistically significant, we observed a slight decrease in the epidermal thickness. Accordingly, FP 0.05% treatment resulted in a significant reduction of PICP expression \( (p = 0.020; \) table 2, online suppl. fig. 3).

Ki-67 is a nuclear non-histone protein that is expressed at low levels in quiescent cells but is increased in proliferating cells [8] and that has been established as a marker of cell proliferation [7]. The expression of Ki-67+ cells in the basal layer of the epidermis indicates no significant differences after placebo treatment, whereas the number of Ki-67+ cells decreased significantly after FP 0.05% treatment (fig. 3b, \( p = 0.042 \), compared to placebo not...
**Fig. 2.** Clinical response to the applied study drugs over time in study A (AD patients). Shown are mean values ± standard deviations; placebo n = 25, GW870086 (GW) 0.2% n = 20, GW 2% n = 15, FP 0.05% n = 15. The method of adjustment of the TIS score is described in the Methods.

**Fig. 3.** Immunohistochemical analysis of skin biopsies before and after treatment (subgroup of 10 AD patients). Placebo n = 10, FP 0.05% n = 7, GW870086 (GW) 0.02% n = 7, GW 2% n = 6. 

- **a** Analysis of epidermal thickness.
- **b** Epidermal proliferating marker Ki-67.
- **c** Infiltrates of CD4+.
- **d** CD8+ T cells. A mean subject level baseline was calculated. Statistical analyses were performed with a non-parametric test for paired data (changes between before and after treatment are shown in the graphs) and for unpaired data (differences between the treatment groups). P = Placebo. * p < 0.007, FP 0.05% versus placebo.
Neither GW870086 0.2% nor GW870086 2% treatment led to significant changes of Ki-67 expression in the basal layer in comparison to baseline or placebo. Lastly, we aimed to determine the impact of corticosteroid treatment on the presence of CD4+ and CD8+ T cells in the skin before and after treatment. We observed a slight reduction of CD4+ T cells after placebo treatment, which was more pronounced, but not statistically significant, after the treatment with FP 0.05% (fig. 3c). The treatment with GW870086 at the 2 different concentrations led also to a slight to moderate decrease in CD4+ T cells in lesional skin, but no statistical significance was reached. The analysis of CD8+ T cells in lesional skin showed that CD8+ cells are much less present in the skin of AD patients, and their frequency per patient’s lesion is highly variable (fig. 3d). Nevertheless, we observed no changes of CD8+ cells in the placebo-treated lesions but a visible reduction after treatment with FP 0.05%, GW870086 0.2% and GW870086 2%, although again without reaching statistical significance.

### Skin Thinning and the Novel Corticosteroid in Healthy Control Subjects (Study B)

The primary analysis of the changes in skin thickness from baseline showed no skin thinning after the application of GW870086 after 42 days of dosing at both concentrations, i.e. 0.2% (−0.01, 95%CI −0.06 to 0.03) and 2% (0.02, 95%CI −0.03 to 0.07) relative to placebo. However, significant skin thinning was observed on days 14 and 21 when treated with CP 0.05%, a highly potent corticosteroid, compared to placebo. The mean change in skin thickness on day 14 was less than on day 21, but already significant (table 3).

### Tolerability and Pharmacokinetics

At every visit, a review of local tolerability was performed. In both studies, no drug-related adverse events (AEs) were reported. Overall, a total of 21 AEs were reported during both studies (study A, 15 AEs; study B, 6 AEs). No AE was judged to be of severe intensity, and no evident changes in safety laboratory parameters were observed in either of the studies over the course of the treatment.

Taking both studies together, 45 subjects were included in the pharmacokinetic population. GW870086 plasma concentrations were not quantifiable (<40 pg/ml) at any point in time in 38 of the 45 subjects up to 24 h postdose on day 21 (study A) or day 42 (study B).

Only 3 AD patients treated with GW870086 0.2%, GW870086 2% and placebo (study A, treatment group 1) displayed single quantifiable values of GW870086 ranging from 51.1 to 55.0 pg/ml. Three healthy control subjects treated with the same study drugs (GW870086 0.2%, GW870086 2% and placebo; study B, treatment group 1) showed single quantifiable values ranging from 40.6 to 52.7 pg/ml, and 1 healthy control subject of the same treatment group had 2 quantifiable values of 88.9 pg/ml on day 14 predose and 759.8 pg/ml on day 42 predose.

### Discussion

We studied the clinical efficacy, tolerability and atrophogenic potential of a novel selective topical corticosteroid, GW870086, at 2 different concentrations in AD patients and healthy control subjects. The data show that the novel corticosteroid had no atrophogenic potential during the observational period (21 and 42 days) and was well tolerated in both cohorts. However, although a dose-dependent reduction of the TIS score was observed over time, no statistical significance in clinical efficacy was achieved in AD patients. By contrast, FP 0.05%, a potent class 3 corticosteroid, shows clear clinical efficacy in comparison to placebo.

Topical corticosteroids have been used >50 years due to their anti-inflammatory action [3, 11]. Attempts have been made to develop novel corticosteroids which are still clinically efficacious but have fewer side effects. Among these second-generation corticosteroids, still significant and clinically relevant side effects can occur [12].

#### Table 2. Analysis of PICP expression (subgroup of 10 AD patients). The analysis was done semiquantitatively using a score between 0 (no expression) and 3 (strong expressions)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median intensity, semiquantitative analysis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n = 10)</td>
<td>2 (1–3) points</td>
<td>2 (1–3) points n.s.</td>
</tr>
<tr>
<td>FP 0.05% (n = 7)</td>
<td>2 (2–3) points</td>
<td>1 (1–2) points 0.020*</td>
</tr>
<tr>
<td>GW 0.2% (n = 7)</td>
<td>2 (2–3) points</td>
<td>2 (1–3) points n.s.</td>
</tr>
<tr>
<td>GW 2% (n = 6)</td>
<td>2 (1–2) points</td>
<td>2 (1–3) points n.s.</td>
</tr>
</tbody>
</table>

Statistical analyses were performed with non-parametric tests for paired data (changes between before and after treatment are shown in the graphs of fig. 3) and for unpaired data (differences between the treatment groups). Values in parentheses denote the minimum to maximum ranges. GW = GW870086; n.s. = non-significant * p = 0.019, FP 0.05% vs. placebo.

*significant. GW870086 0.2% treatment led to significant changes of Ki-67 expression in the basal layer in comparison to baseline or placebo. GW870086 2% treatment led to significant changes of Ki-67 expression in the basal layer in comparison to baseline or placebo.

Topical corticosteroids have been used >50 years due to their anti-inflammatory action [3, 11]. Attempts have been made to develop novel corticosteroids which are still clinically efficacious but have fewer side effects. Among these second-generation corticosteroids, still significant and clinically relevant side effects can occur [12].
Therefore, the identification of more selective corticosteroids based on molecular mechanisms dissecting transactivating and transrepressive activities at the genomic level has been the focus of development [3].

The novel corticosteroid used here was extensively examined via different models both preclinically and clinically [5, 6]. The data consistently indicated anti-inflammatory activity similar to that seen with traditional corticosteroids. More recently, the results of an allergen challenge study in 24 mild asthmatics showed a significant anti-inflammatory activity that was close to FP (late asthmatic response and methacholine challenge) [7]. However, the data indicated that GW870086 may be between 3 and 10 times less potent than FP, hence requiring a higher dose to match traditional steroids. These results therefore suggest an improved therapeutic index for GW870086.

We were able to perform some mechanistic analysis including the measurement of cellular activation markers, the presence of T cell infiltrates and the determination of epidermal/dermal atrophic changes. The reduction of epidermal thickness was associated with clinical efficacy by using hydrocortisone, as we have shown previously [13]. An initial step of skin atrophy is the reduction in epidermal thickness followed by dermal atrophic changes. The first-mentioned effect was only seen after FP 0.05% treatment accompanied by a decrease in cell size characterising atrophogenicity [14]. In addition, GW870086 treatment might be normalising the epidermal thickness without atrophic qualities. The latter effect results from a direct antiproliferating effect of corticosteroids on fibroblast activity. This effect causes a reduced collagen synthesis resulting in skin atrophy and promoting the onset of telangiectasia [11]. Collagen is a major dermal protein which provides skin tautness [11]. It mostly comprises collagen type I [15]. As a precursor of collagen type I, PICP is synthesised by fibroblasts. Its expression reflects the de novo synthesis of collagen type I [16, 17]. We assessed the expression of PICP in lesions before and after treatment to delineate the atrophogenic potential of the molecules used. We indeed observed a significant reduced expression of this molecule after FP 0.05% treatment, but not upon treatment with the novel corticosteroid, supporting the data assessed by ultrasound analysis in healthy skin.

T helper cells play a crucial role in the pathogenesis of AD [17]. The exploratory analysis of T-cell infiltrates after the 3-week course of treatment with FP 0.05% shows a visible reduction of both CD4+ and CD8+ T cells, although not being statistically significant. It is still not known whether any changes of the T-cell infiltrates during a 3-week course of treatment are due to changes of T-cell survival or due to changes of T-cell migration into skin. This can be studied in more detail by sequential biopsies during treatment; however, for ethical reasons such studies in humans are limited. Although we did not measure any cytokines in the lesions of our AD patients, the changes in the cellular infiltrates suggest that the novel corticosteroid treatment most likely led to changes of the cytokine milieu as well. An analysis of the local cyto-

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**Table 3.** The new selective corticosteroid does not cause skin thinning in healthy control subjects. A negative value is indicative of skin thinning, whereas a positive value represents skin thickening

<table>
<thead>
<tr>
<th>Treatment comparison</th>
<th>Treatment day</th>
<th>Difference in adjusted means</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP 0.05% vs. placebo</td>
<td>14</td>
<td>-0.1506 (0.0381)</td>
<td>-0.2297 to -0.0716</td>
<td>0.0007</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>-0.1770 (0.0388)</td>
<td>-0.2600 to -0.0939</td>
<td>0.0004</td>
</tr>
<tr>
<td>GW 0.2% vs. placebo</td>
<td>14</td>
<td>-0.0271 (0.0227)</td>
<td>-0.0730 to 0.0188</td>
<td>0.2395</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>-0.0035 (0.0225)</td>
<td>-0.0490 to 0.0420</td>
<td>0.8767</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>0.0008 (0.0225)</td>
<td>-0.0450 to 0.0467</td>
<td>0.9715</td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>-0.0130 (0.0212)</td>
<td>-0.0563 to 0.0303</td>
<td>0.5446</td>
</tr>
<tr>
<td>GW 2% vs. placebo</td>
<td>14</td>
<td>0.0015 (0.0240)</td>
<td>-0.0469 to 0.0500</td>
<td>0.9490</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>0.0129 (0.0237)</td>
<td>-0.0351 to 0.0609</td>
<td>0.5894</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>0.0268 (0.0237)</td>
<td>-0.0216 to 0.0751</td>
<td>0.2681</td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>0.0201 (0.0223)</td>
<td>-0.0256 to 0.0657</td>
<td>0.3764</td>
</tr>
</tbody>
</table>

CP 0.05% n = 5, placebo n = 20, GW870086 (GW) 0.2% n = 15, GW 2% n = 20. Values in parentheses denote standard error.

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Corticosteroids and Atopic Dermatitis

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kinine profile upon treatment should be considered in future studies, including an analysis of classic memory T cell cytokines, such as IL-4, IL-13 and INF-γ, but also of recently described factors, such as thymic stromal lymphopoietin [18], IL-31 [19], IL-22 or IL-17 [20, 21].

No safety concerns were raised during the course of the 2 studies. Because of the study design (50 mg of each study drug restricted to small skin areas), it was not possible to monitor or interpret systemic side effects due to GW870086 plasma levels.

In summary, we show that local application of the novel selective corticosteroid GW870086 does not display a clinical efficacy superior to placebo. GW870086 showed no signs of atrophogenic effects in AD patients as well as in healthy control subjects during the observed period of time. The clinical efficacy achieved in this study was not superior to placebo, although dose-dependent effects of the substance were noticed. It needs to be taken into consideration that our study had clear limitations, as only single lesions were treated instead of affected body surface areas. Furthermore, clinical studies considering these aspects may be worthwhile to explore the efficacy and tolerability of GW870086.

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