

Efficacy and tolerance assessment of a new type of dermocosmetic in infants and children with moderate atopic dermatitis

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Summary

Background Atopic dermatitis (AD) is an inflammatory and pruritic skin disorder.

Objectives To assess the efficacy and tolerance of a new emollient (SBT complex) in subjects with moderate AD.

Methods Subjects received twice daily for 168 days (6 months) either SBT complex or emollient base adjunctively or alternately with topical corticosteroids or calcineurin inhibitors. Evolution of AD was assessed throughout the study using usual AD assessment criteria including SCORAD and PO-SCORAD. Quality of life was assessed at Day 0 and Day 168.

Results At Day 168, a significant decrease with SBT complex was observed for the SCORAD and the PO-SCORAD scores ($P < 0.05$), the primary efficacy criteria. A total of 76% of SBT complex subjects did not relapse and time-to-relapse increased compared to the emollient base subjects. Intensity, dryness, and quality of life ($P < 0.05$) had improved in subjects using SBT complex. The product was well tolerated with less physical and functional signs in the SBT than in the emollient base group.

Conclusion The new emollient dermocosmetic SBT complex applied adjunctively or alternately with topical AD treatments significantly improved AD without any safety concerns. SBT complex may play an important role in the restoration of the natural skin barrier.

Keywords: Atopic dermatitis, quality of life, SBT complex, skin barrier

Introduction

Atopic dermatitis (AD), or eczema, is a common inflammatory and pruritic skin disorder that frequently appears in early childhood and may continue into later life.^{1–3} It is marked by alternating periods of exacerbations and remissions with up to 20% of school-aged children being affected. AD profoundly influences the patients' quality of life and that of their families.^{4–8}

To date, topical corticosteroids and topical calcineurin inhibitors are the main topical treatments in AD.⁹ Both are efficient in infants, children, and adult patients. In addition, and for increased patient comfort, the importance of the so-called basic therapy with emollients is currently required in clinical practice as it rehydrates and smoothens the skin.¹⁰

In this study, we tested the efficacy and safety as an adjunctive to current topical AD treatments of a new emollient dermocosmetic (hereafter SBT complex for Skin Barrier Therapy, marketed as Atoderm® Intensive cream, Laboratoire Bioderma, France) compared to its emollient base containing glycerin at 2% and stearic acid.

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SBT complex contains vitamin B3 Palmitoyl Ethanolamide (PEA) an antipruritus agent, sucroesters, β -sitosterol an anti-inflammatory agent and zinc known for its antibacterial action against *Staphylococcus aureus* known for triggering AD.¹¹ Preliminary, nonpublished studies have shown that SBT complex containing Vitamin B3 helps to restore biologically the natural skin barrier by inducing the synthesis of epidermal lipids and by reinforcing the action on the skin barrier.

SBT complex uses a multilamellar lipidic complex enhancing the integration into the skin of ceramides, lacking in AD skin, as well as other active substances, thus restoring the deficient natural skin barrier.

Methods

Study design and population

Between March 2012 and June 2013, one investigator in Poland conducted a randomized, double-blinded, and comparative study. The study was performed according to the Declaration of Helsinki of 1976 and its successive updates, the Good Clinical Practices for the conduct of clinical trials, and local ethical requirements. Prior to any inclusion, subjects' caregivers and, depending on the age, the subjects provided written informed consent. Male or female children with no reported history of allergy and aged from 6 months to 15 years with an AD severity score of 15–40 on the SCORAD scale at selection visit having suffered from 3 to 6 eczema flare-ups during the 6 months prior to the study and presenting at least one flare-up at selection visit were suitable for inclusion.

Treatments

Subjects were randomized at the investigational site in a 1:1 way and received either SBT complex or its emollient base on the whole of their body with a twice-daily application over a period of 168 days (6 months) alternately or adjunctively to their conventional topical AD treatment (topical corticosteroids or calcineurin inhibitors such as pimecrolimus or tacrolimus). AD treatments were prescribed at selection visit, prior to entering the study. Subjects were not allowed to alter their prescribed AD medication regimen and to continue concomitantly their current emollient or moisturizing products. The concomitant use of inhaled corticosteroids, antihistamines, and hygiene products was permitted.

Assessments

SCORAD and PO-SCORAD scores, the primary efficacy criteria as well as dryness and treatment type were reported at inclusion visit (Day 0), after 56 (Day 56), 112 (Day 112), and 168 days (Day 168). Relapse (flare-up) rate, severity, and time-to-first relapse as well as treatment duration were assessed at Day 56, Day 112, and Day 168. The investigator calculated the SCORAD and PO-SCORAD scores assessed by the child's caregivers and by the child at these visits. The children's and parents' quality of life using the Infants Dermatitis Quality of Life Index (IDQOL), Children's Dermatology Life Quality Index (CDLQI), Dermatitis Family Impact (DFI) were rated at Day 0 and after 6 months on a scale from 0 to 1 = no effect at all on patient's life, 2–5 = small effect on patient's life, 6–10 = moderate effect on patient's life, 11–20 = very large effect on patient's life to 21–30 = extremely large effect on patient's life. Subjects' efficacy and cosmetic perception were rated after 6 months. Overall, safety and local tolerance were assessed throughout the study. The number of days during which topical corticosteroids, calcineurin inhibitors, or antihistamines were applied as reported by the subjects served to calculate the mean number of treatment days for both groups. The incidence was calculated separately for subjects receiving topical corticosteroids, calcineurin inhibitors, or antihistamines. Dryness was assessed at all visits using a score 0 (absent) to 3 (severe).

Statistics

Categorical variables including subject perception were summarized by frequency and percentage for each category. Quantitative and semi-qualitative variables were summarized. A generalized estimating equation model was used to assess the difference in the number of relapses and to evaluate skin dryness as well as quality of life.

Analyses of the SCORAD and PO-SCORAD scores were performed using the ANOVA model. The comparison between treatment groups was assessed using the Mann–Whitney *U*-test. The type I error was set at $\alpha = 0.05$ in a two-tailed approach.

The sample size was calculated to show a 25% difference of severity between the two groups.

Results

Demographic and baseline data

A total of 123 subjects were analyzed in this study: 62 subjects in the SBT complex and 61 in the emollient

Table 1 Demographics and Baseline data

Parameters	Value	
	SBT complex	Emollient base
N (%)	62 (100%)	61 (100%)
Age (years)		
Mean $\pm$ SD	4.0 $\pm$ 0.0	6.0 $\pm$ 1.0
Gender		
Male	34 (54.8%)	33 (54.1%)
Female	28 (45.2%)	28 (45.9%)
Phototype		
I	10 (16.1%)	10 (16.4%)
II	37 (59.7%)	35 (55.7%)
III	5 (8.1%)	6 (9.8%)
IV	10 (16.1%)	11 (18.1%)
Topical AD treatments		
Corticosteroids	20 (17.4%)	26 (22.6%)
Calcineurin inhibitors	10 (8.7%)	16 (13.9%)
SCORAD (at selection)	26.5 $\pm$ 0.9	26.4 $\pm$ 1.0
PO-SCORAD (at selection)	32.1 $\pm$ 1.9	32.4 $\pm$ 1.7

base group. Demographic and baseline data in both treatment groups were well balanced with no notable difference. Table 1 provides detailed demographic and baseline data.

Efficacy

SCORAD and PO-SCORAD

After 168 days of use, the SCORAD score in the SBT complex group had significantly ($P < 0.05$) decreased from 7.2 ± 0.6 at Day 0 to 3.5 ± 0.8 , while it remained unchanged (7.2 ± 0.6 vs 7.2 ± 1.1) in the emollient base group. The percent decrease at Day 168 from Day 0 is shown in Figure 1.

At the same time point, the PO-SCORAD score had significantly decreased from 10.4 ± 9.1 at Day 0 to 4.7 ± 8.5 in the SBT group and from 9.1 ± 5.5 to 7.7 ± 9.0 in the emollient base group (both $P \leq 0.01$). In the SBT group, the difference to Day 0 was statistically significant as early as Day 56. The difference compared to Day 0 was statistically significant in the emollient base group at Day 168, only.

The difference between the SBT complex group and the emollient base group was significant at Day 112 and Day 168 (both $P \leq 0.05$). Figure 2 provides the percent decrease at Day 168 for both groups.

Relapse rate during the 6 months preceding the study, all subjects had at least 3 relapses reported. After 168 days of use, 44 (76%) subjects in the SBT complex group had no relapse reported anymore.

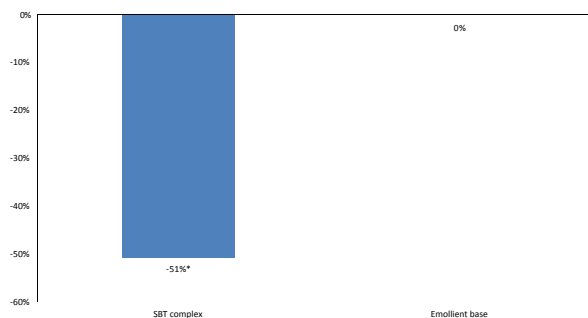


Figure 1 Percent decrease of SCORAD rates after 168 days of twice-daily applications. *: $P < 0.05$ compared to the emollient base.

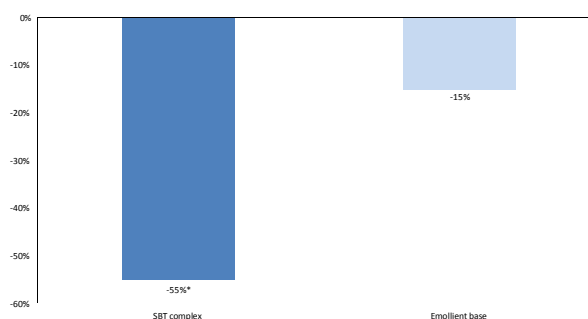


Figure 2 Percent decrease of PO-SCORAD rates after 168 days of twice-daily applications. *: $P < 0.01$ compared to the emollient base.

Conversely, only 39 (68%) subjects in the emollient base group had no relapse reported. During the 168 days of use, only one (2%) subject had 3 or more relapses recorded with SBT complex compared to 4 (7%) subjects using the emollient base.

Severity and time-to-first relapse

With a mean SCORAD value of 17.8 ± 1.7 , the severity of the first relapse was less important in the SBT complex group than it was in the emollient base group (21.3 ± 1.9 days). Overall, severity of relapses had decreased by 49% in SBT complex group compared to 15% in the emollient base group. The mean time-to-first relapse was 59 ± 11 days in the SBT complex group and 39 ± 12 days in the emollient base group.

Drug administration duration

During relapses, the mean number of treatment days with corticosteroids was almost similar in both groups (4.3 ± 1.1 vs. 4.8 ± 1.0 days for the SBT complex and emollient base, respectively). Conversely, the mean

duration of use of calcineurin inhibitors in the SBT complex group was lower (1.6 ± 0.6 days) compared to that in the emollient base group (3.8 ± 1.0 days) corresponding to a difference of 58%.

Concomitantly taken antihistamines to reduce pruritus were less often used by subjects in the SBT group (0.5 ± 0.3 days) than by subjects in the emollient base group (3.5 ± 1.6 days). The 86% difference was statistically significant ($P < 0.05$).

Dryness

At Day 0, 52 (83.9%) subjects in the SBT complex and 50 (81.9%) subjects in the emollient base group reported dry skin. At Day 56 and Day 112, a significant decrease (all $P \leq 0.05$) of the number of subjects with dry skin was observed in the SBT complex group (35; 57% and 25; 40%, respectively) compared to the emollient base group (48; 75% and 38; 63%, respectively). After 168 days, the difference was almost significant ($P = 0.0518$): only 17 (28%) subjects in the SBT complex compared to 27 (44%) subjects in the emollient base group still reported dry skin. Figure 3 shows the percent decrease of skin dryness over time in both groups.

Quality of life

Children under the age of four. A total of 47 subjects in the SBT complex and 36 in the emollient base group replied to the IDQOL questionnaire. At Day 0, the skin condition in the SBT complex group impacted moderately (5.5 ± 0.9) on the subjects' quality of life and only had a slight impact (3.7 ± 0.7) in the emollient base group.

At Day 168, AD no longer had an impact (0.6 ± 0.3) on the subjects' quality of life in the SBT complex group. Conversely, the emollient base did not notably improve the subjects' quality of life

(2.7 ± 0.8). The difference was significant ($P < 0.05$) between both groups in favor for the SBT group.

Children above the age of four. Fifteen (15) subjects in the SBT complex group and 25 in the emollient base group answered the CDLQI questionnaire. At Day 0, AD only slightly affected the subjects' quality of life (2.5 ± 0.5 and 2.3 ± 0.5 in the SBT complex and emollient base group, respectively). After 168 days of treatment, a significant decrease of the CDLQI global score compared to Day 0 was observed in the SBT complex group (1.8 ± 0.7 , $P = 0.01$) and in the emollient base group (1.8 ± 0.5 , $P < 0.0001$). There was no difference between both groups after 168 days.

Family quality of life. A DFI questionnaire was completed by all subjects. The global impact index on the family was calculated from the sum of all answers provided by each subject. Even if AD at Day 0 only had a small impact on the families' quality of life in both groups (4.8 ± 0.5 and 3.1 ± 0.4 for the SBT complex and for emollient base group, respectively), an improvement could still be observed after 168 days. This improvement was more important ($P < 0.05$) with SBT complex (0.4 ± 0.5) than with the emollient base (0.9 ± 0.6). Table 2 provides an overview of all efficacy results.

Safety and local tolerance

A total of 4 subjects (6.5%) in the SBT complex group reported functional or physical signs possibly or definitively related to SBT complex – these events comprised warm sensation, pruritus, stinging, pain, erythema, and flare-ups – compared to 7 (11.4%) subjects in the emollient base group. In the latter group, 6 subjects reported pruritus; one subject had a short period of severe pruritus followed by moderate pruritus; and a second one reported moderate pruritus. One subject reported a mild warm sensation. Physical signs in subjects who used the emollient base included mild flare-ups, mild or moderate erythema and papules.

One subject in the SBT complex group withdrew from the study due to intolerance to the product characterized by slight erythema on the back.

Discussion

With the present study, we demonstrated for the first time that a new emollient dermocosmetic containing SBT complex, applied on a daily basis adjunctively or alternately to conventional topical AD treatments over

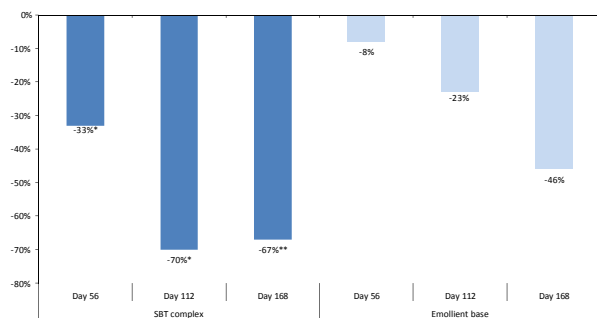


Figure 3 Percent decrease of skin dryness over time after twice-daily applications. *: $P < 0.05$ compared to the emollient base. **: $P = 0.0518$ compared to the emollient base.

Table 2 Overview of efficacy results after 168 days of use of SBT complex or emollient base

Efficacy criteria	SBT complex	Emollient Base	Significance
Primary efficacy criteria			
SCORAD (Day 0 vs Day 168)	7.2 ± 0.6 vs 3.5 ± 0.8 (–51%)	7.2 ± 0.6 vs 7.2 ± 1.1 (0%)	<i>P</i> < 0.05
PO-SCORAD (Day 0 vs Day 168)	10.4 ± 9.1 vs 4.7 ± 8.5 (–55%)	9.1 ± 5.5 vs 7.7 ± 9.0 (–15%)	<i>P</i> < 0.05
Secondary efficacy criteria			
Relapse rate (no. subjects)			
No relapses	44 (76%)	39 (68%)	Not significant
3 relapses or more	1 (2%)	4 (7%)	Not significant
Severity of first relapse (SCORAD)	17.8 ± 1.7	21.3 ± 1.9	Not significant
Time to first relapse (days)	59 ± 11	39 ± 12	Not significant
AD treatment duration during relapses (days)			
Corticosteroids	4.3 ± 1.1	4.8 ± 1.0	Not significant
Calcineurin inhibitors	1.6 ± 0.6	3.8 ± 1.0	Not significant
Antihistamines	0.5 ± 0.3	3.5 ± 1.6	<i>P</i> < 0.05
Dryness (no. subjects)			
Day 0	52 (83.9%)	50 (81.9%)	–
Day 168	17 (28%)	27 (44%)	<i>P</i> = 0.0518*
Quality of life (Day 0 vs Day 168)			
<4 years	5.5 ± 0.9 vs 0.6 ± 0.3	3.7 ± 0.7 vs 2.7 ± 0.8	<i>P</i> < 0.05
>4 years	2.5 ± 0.5 vs 1.8 ± 0.7	2.3 ± 0.5 vs 1.8 ± 0.5	Not significant
Family QoL	4.8 ± 0.5 vs 0.4 ± 0.5	3.1 ± 0.4 vs 0.9 ± 0.6	<i>P</i> < 0.05

*Almost significant.

a period of 168 days on infants and children with moderate AD provided a significant improvement of AD symptoms when compared to a simple moisturizing and smoothening emollient. Indeed, formulated in an emollient glycerin preparation at 2%, SBT complex contains active ingredients allowing reducing pruritus, inflammation and vitamin B3, known for its potential for restoring the barrier function of healthy skin over the long term by inducing the synthesis of epidermal lipids and by reinforcing the action on the skin barrier in reducing dryness.^{12,13} The assessment of SCORAD and PO-SCORAD scores after 168 days of use provided evidence of a statistically significant improvement compared to the emollient base, a decreased number, and severity of relapses, and of a prolonged time-to-relapse. Additionally, the novel emollient dermocosmetic allowed for a significantly reduced concomitant use of antihistamines and, to a less important extent, calcineurin inhibitors. The latter is especially of importance as the prolonged use of calcineurin inhibitors may bear a risk of lymphoma as pointed out by the FDA.¹⁴ Even though their role in the management of pruritus in AD is controversial,^{15,16} the reduced concomitant use of antihistamines may suggest a decreased level of allergies, hence, confirming a close relationship between AD, allergies, and pruritus.

Cosmetic acceptability of the new emollient dermocosmetic was high (data not shown) which is most

important as emollients have a recognized role in the daily management of AD and in treatment compliance.¹⁷ Assessment of quality of life confirmed that the proposed novel emollient dermocosmetic allows patients and their caregivers to improve not only their AD but also their well-being and that of their families. Safety of the emollient dermocosmetic containing SBT complex was good.

We agree that the sample size and the single-center study design may lead to limitations. Furthermore, we agree that pruritus, one of the main symptoms of AD, should have been assessed independently at all study visits. However, this symptom was assessed using the patient questionnaire, showing that pruritus had improved after 168 days of use of SBT complex compared to its emollient base. Despite this weakness, we consider that the efficacy and safety outcome of this study demonstrated that the proposed novel emollient dermocosmetic containing SBT complex allows for an additional and safe pain and burden relief in infants and pediatric patients with AD when used adjunctively or alternately with topical corticosteroids or calcineurin inhibitors.

In conclusion, the novel emollient dermocosmetic containing SBT complex efficiently decreased the SCORAD and PO-SCORAD, as well as the severity of dryness, the main sign of AD. The emollient dermocosmetic was safe and well perceived by the subjects and their caregivers while study results suggest

that SBT complex may play a role in the restoration of the natural skin barrier damaged by AD.

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