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MAS063DP (Atopiclair®) for the Treatment of Atopic Dermatitis in Infants and Children: Proceedings of a Roundtable Discussion

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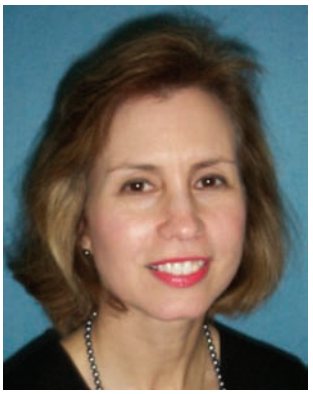

The science of atopic dermatitis has come a long way in the last few years. While today, dermatologists are using the term *barrier dysfunction*, it was not something that specialists discussed two or three years ago, even though it was known that there was a barrier defect that required ongoing management. A growing need for nonsteroidal therapy for atopic dermatitis exists, especially for infants and children. Nonsteroidal barrier repair is currently being intensely researched. An important recent study involves a nonsteroidal, barrier repair cream by the name of Atopiclair® (Graceway Pharmaceuticals, LLC, Bristol, Tennessee). The following clinical review discusses a multicenter, randomized, placebo-controlled study evaluating the efficacy and safety of Atopiclair in infants and children with mild-to-moderate atopic dermatitis. The study demonstrated that Atopiclair cream is effective and safe as a monotherapy for the treatment of symptoms of mild-to-moderate atopic dermatitis in infants and children. Mark Boguniewicz, MD, of the National Jewish Medical and Research Center in Denver, Colorado, was the lead investigator for this important pediatric study.[1]

Adelaide A. Hebert, MD, is Professor of Dermatology and Pediatrics at the University of Texas—Houston Medical School, in Houston, Texas. Dr. Hebert is board certified in dermatology, pediatric dermatology, and wound healing. Her medical training includes a fellowship in pediatric dermatology at Northwestern University. She joined the dermatology faculty of UT Houston in 1986.

This supplement is based on a roundtable discussion that took place on June 28, 2008, at the Sandestin Beach Hilton Hotel in Sandestin, Florida. Dr. Hebert moderated the discussion. Roundtable participants included Drs. Baum, Del Rosso, Dwyer, Eastern, and Herron. This supplement was supported by Graceway Pharmaceuticals and did not undergo peer review by *The Journal of Clinical and Aesthetic Dermatology's* Editorial Advisory Board.

MAS063DP (Atopiclair®) for the Treatment of Atopic Dermatitis in Infants and Children

Proceedings of a Roundtable Discussion

Introduction

On June 28, 2008, a roundtable discussion was held to review the management of atopic dermatitis in pediatric patients. This roundtable took place during the Alabama Dermatological Society meeting in San Destin, Florida. Dr. Adelaide Hebert, Professor of Dermatology and Pediatrics at the University of Texas Houston Medical School—Houston, Texas, served as chair and moderator of the session. A primary objective of the session was to discuss recently published data on the use of a nonsteroidal topical barrier repair cream that contains glycyrrhetinic acid 2%, hyaluronic acid, *Vitis Vinifera* extract (grapevine), telmesteine, and *Butyrospermum parkii* (shea butter), and is marketed under the trade name Atopiclair (Graceway Pharmaceuticals, LLC, Bristol, Tennessee).

A multicenter, randomized, vehicle-controlled study recently published in the June 2008 issue of the *Journal of Pediatrics* evaluated the use of Atopiclair as monotherapy for mild-to-moderate atopic dermatitis in infants and children. This multicenter, randomized, placebo-controlled, 43-day study included 142 subjects. Mark Boguniewicz, MD, of the National Jewish Medical and Research Center in Denver, Colorado, served as lead investigator. Atopic dermatitis was assessed to cover at least five-percent body surface area for all patients at study entry, with evaluations occurring at baseline and Days 3, 8, 15, 22, 29, and 43. The primary endpoint of this pediatric study was Investigator Global Assessment (IGA) of atopic dermatitis at Day 22. Secondary endpoints included IGA at other time points, patient's/caregiver's assessment of pruritus, onset, duration of itch relief, Eczema Area and Severity Index (EASI), subject's/caregiver's assessment of global response, and need for rescue medication (such as a topical corticosteroid) in the event of an atopic dermatitis flare. Atopiclair cream was statistically more effective ($P<0.0001$) than vehicle cream for the primary endpoint and all secondary endpoints and proved to be safe and well tolerated. The results of this pediatric study were compared to those reported in a previous study completed in adult subjects.

The roundtable discussion was not limited to the results of the pediatric trial summarized above. Other issues that were addressed included management of epidermal barrier dysfunction, trigger factors for atopic dermatitis, superimposed bacterial infections, and associated behavioral and emotional sequelae of the disease. In addition to Dr. Hebert, who served as chair and moderator, other roundtable discussion participants included Eric W. Baum, MD; Joseph S. Eastern, MD; Gregory A. Dwyer, MD; and Mark D. Herron, MD.

We are hopeful that the information presented in this roundtable proceedings will be helpful to you in clinical practice.

James Q. Del Rosso, DO, Editor-in-Chief, Clinical Dermatology, The Journal of Clinical and Aesthetic Dermatology

Atopiclair is Effective Monotherapy for Mild to Moderate Atopic Dermatitis in Infants and Children:

A Multicenter, Randomized, Vehicle-controlled Study

Boguniewicz M, Zeichner JA, Eichenfield LF, et al. MAS063DP is effective monotherapy for mild to moderate atopic dermatitis in infants and children: a multicenter, randomized, vehicle-controlled study.
J Pediatr. 2008;152(6):854-859.

Study Highlights

Objective. To examine the efficacy and safety of Atopiclair cream in the management of mild-to-moderate dermatitis in infants and children.

Study design. One-hundred forty-two patients aged six months to 12 years were administered Atopiclair (n=72) or vehicle (n=70) cream three times per day to affected areas and sites prone to develop atopic dermatitis. The primary endpoint for efficacy was the Investigator's Global Assessment at Day 22. Secondary endpoints included IGA at other time points, patient's/caregiver's assessment of pruritus, onset, duration of itch relief, Eczema Area and Severity Index (EASI), subject's/caregiver's assessment of global response, and need for rescue medication (such as a topical corticosteroid) in the event of an atopic dermatitis flare.

Results. Atopiclair cream was statistically more effective ($P<0.0001$) than vehicle cream for the primary endpoint and all secondary endpoints. Treatment discontinuation as a result of an adverse event occurred in 9.9 percent of patients using Atopiclair cream and 16 percent of patients using vehicle cream.

Conclusion. Atopiclair cream is effective and safe as monotherapy for the treatment of symptoms of mild-to-moderate atopic dermatitis in infants and children.

Roundtable Discussion

What was the objective of the recently published Atopiclair pediatric trial?

Atopic dermatitis has a complex etiology that encompasses many genetic as well as environmental triggers that compromise skin-barrier function. As a result of our understanding of the pathophysiology of atopic dermatitis increasing in recent years, newer therapeutic options such as Atopiclair have become available that may significantly improve quality of life for infants and children with atopic dermatitis. The objective of the pediatric trial was to examine the efficacy and safety of Atopiclair cream in the management of mild-to-moderate atopic dermatitis in infants and children.

What are the components of Atopiclair? How did the vehicle differ in the study?

Atopiclair is a nonsteroidal, hydrolipidic cream that helps maintain a healthy epidermal barrier while providing symptomatic relief of pruritus. The vehicle control in this pediatric study did not include such components as glycyrrhetinic acid 2% (GrA), *vitis vinifera* extract, or *telmestine*, which are ingredients in Atopiclair.[1]

Atopiclair Ingredients	Vehicle Ingredients
Glycyrrhetinic acid 2%	*Emollient base similar to that of Atopiclair, without key ingredients including:*
Hyaluronic acid	
Vitis vinifera extract (grapevine)	Glycyrrhetinic acid 2%
Telmestine	*Vitis vinifera* extract (grapevine)
Butyrospermum parkii (shea butter)	Telmestine

GrA 2%, the active metabolite in licorice root extract, shows anti-inflammatory and antipruritic activity and has been shown to block the degradation of endogenous cortisol through inhibition of 11-ß-hydroxysteroid dehydrogenase.[2] Additionally, GrA potentiates cutaneous hydrocortisone activity responsible for metabolizing hydrocortisone within the skin.[3] The standardized *vitis vinifera* extract in Atopiclair has antioxidant and antiprotease activity, which helps protect against breakdown of the epidermis.[4] Telmestine has antiprotease action and inhibits elastase, collagenase, and matrix metalloproteinase, which are expressed at high levels in patients with atopic dermatitis.[5]

Finally, hyaluronic acid in the emollient helps to hydrate the epidermis and restore barrier function. The hyaluronic acid component is a naturally occurring glycosaminoglycan and is part of the ground substance of connective tissue, which immediately smoothes skin upon application and, as a naturally occurring substance, creates no immunogenic response.[6] The hyaluronic acid component may play a key role in wound healing by enhancing epithelial cell migration as well as differentiation and has an organizational effect within collagen bundles. Hyaluronic acid plays many essential roles in the formulation and maintenance of the skin as an effective barrier. Considered one of the most powerful moisturizing agents known, hyaluronic acid has the extraordinary ability to attract, retain, and transport water. Hyaluronic acid is able to take on and hold greater than $1x10^3$ of its own weight in water. As a unique compound within the skin, it is beneficial when used on very dry skin, such as that seen in patients who manifest atopic dermatitis. Hyaluronic acid—with properties that allow it to immediately smooth the skin—is considered to be nonimmunogenic.[7]

Atopiclair contains shea butter, which is derived from *butyrospermum parkii* trees found in northern Africa. This ingredient is in many over-the-counter products such as soaps and creams. Shea butter, an excellent source of saturated fatty acids and monounsaturated fatty acids as well as linoleic acid and sebum, is incorporated into Atopiclair as an essential ingredient to restore skin barrier function. Distinguishing that shea butter does not come from a legume (i.e., a peanut) and is not in the same allergen class as peanuts is important. Shea butter is protein-free and has not been shown to cause anaphylactic reactions in patients who are allergically sensitive. Shea butter content of Atopiclair was analytically tested and was found to be protein free.[1] Patients with a known allergy to nuts or nut oils should con-

sult their doctor before using this topical preparation.

All of these components are considered important ingredients in reducing inflammation and have other key actions that help the barrier and reduce the likelihood of ongoing atopic dermatitis.

Why is Atopiclair considered a medical device?

The mechanism of action of Atopiclair does not depend on metabolic activity. Therefore, this topical preparation meets the US Food and Drug Administration (FDA) definition for medical device.[8] Atopiclair is the first prescription medical device cleared by the FDA for relief of symptoms (itch, burning, and pain) of atopic and allergic contact dermatitis.[9,10]

What comprised the patient population enrolled in the pediatric trial?

The pediatric trial was allowed to enroll male and female infants and children as young as six months of age to 12 years. There were 142 subjects enrolled at 7 centers across the United States. Of enrolled subjects, 52 percent were female and 48 percent were male. The majority of the pediatric subjects were Caucasian (49% of the patients enrolled), 25 percent were African American, 16 percent were Hispanic, and 10 percent were other (Table 1). In this patient population, the randomization of Atopiclair to vehicle was 1:1, which is different than the adult Atopiclair study where the randomization was 2:1.[1,7]

In the pediatric study, 80 percent of those enrolled had a family history of atopy, including asthma, allergic rhinitis, or atopic dermatitis. Atopic dermatitis and asthma have been shown to correlate clinically. Although the development of asthma in an individual has both genetic and environmental components, the patient population of this trial reveals the same trend toward more high affinity immunoglobulin E (IgE) receptors, since 45 percent of the actual patients enrolled in this pediatric clinical trial also suffered from asthma and/or allergic rhinitis.[1]

Table 1. Subject Demographics and Disease Characteristics at Enrollment

	Atopiclair (N=72)	Vehicle (N=70)
Sex		
Female	36 (50.0%)	38 (54.2%)
Male	36 (50.0%)	32 (45.7%)
Age (years)		
No. of patients	72	70
Mean (SD)	4.89 (3.35)	5.10 (3.29)
Min | Median | Max	0.5 | 4.1 | 11.9	0.6 | 4.5 | 12.5
Ethnic origin		
Black	16 (22.2%)	19 (27.1%)
Hispanic	12 (16.6%)	10 (14.2%)
Caucasian	39 (54.1%)	30 (42.9%)
Other	5 (6.8%)	11 (22.4%)
Pattern of disease		
Constant	44 (61.1%)	42 (60.0%)
Frequent	15 (20.8%)	20 (28.6%)
Intermittent	13 (18.0%)	8 (11.4%)
IGA of AD (score)		
Mild	37 (51.3%)	37 (52.8%)
Modrate	35 (48.6%)	33 (47.1%)
Itch (VAS score, mm)		
No. of patients	72	70
Mean (SD)	61.89 (16.99)	67.41 (17.24)
Min | Median | Max	40 | 60 | 00	40 | 70 | 00

*Data missing for one patient.

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What were the patterns of atopic dermatitis in the pediatric population of this trial?

In the pediatric study, 66 of the patients (60.6%) had constant atopic dermatitis. Additionally, 35 of the 142 patients' (24.6%) atopic dermatitis was described as being frequent. Only 21 of the study entrants' atopic dermatitis was described as being intermittent. This constituted 14.8 percent of all the patients enrolled.

In terms of atopic dermatitis severity, there were 37 patients in the Atopiclair arm and 37 patients in the vehicle arm that had mild atopic dermatitis. By comparison, there were 35 patients in the Atopiclair arm and 33 in the vehicle group who were determined to have moderate disease. Atopic dermatitis was assessed to cover at least five-percent body surface area for all patients at study entry.

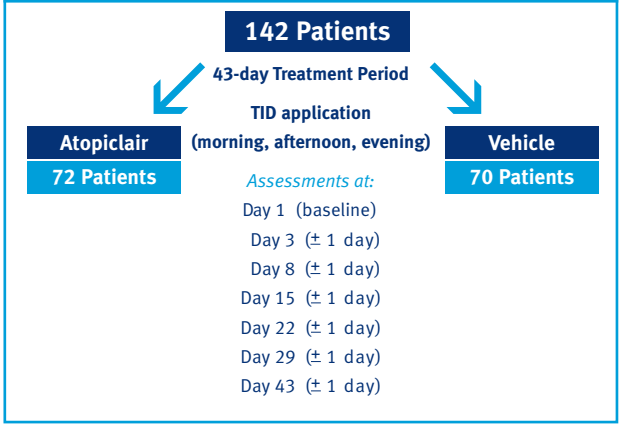
What was the study design for the Atopiclair pediatric trial?

The pediatric trial began with a washout period, just as was required in the adult trial. Patients and caregivers agreed to refrain from using other topical and systemic medications as well as phototherapy during the washout and study periods. A washout period of seven or 14 days was used for patients on topical and systemic medications, respectively, including topical and systemic corticosteroids, topical calcineurin inhibitors, antihistamines, and phototherapy. As in the adult trial, if clinically indicated, a low potency rescue topical steroid was prescribed for patients by the study investigator if a flare occurred during the course of the study that warranted medical intervention.

Eligible subjects were randomized to receive either Atopiclair or vehicle control in a 1:1 ratio. The pediatric trial was a 43-day study with assessments at baseline and Days 3, 8, 15, 22, 29, and 43. The patients, or parents, were instructed to apply the cream morning, afternoon, and evening using a three-times-daily application **(Figure 1)**.

The ingredients in Atopiclair that were eliminated in the vehicle were GrA, *vitis vinifera* (grapevine) extract, and telmestine. In this pediatric study batch, the Atopiclair lot was tested for the presence of shea nut protein and none was detected.[1]

Figure 1. Pediatric Trial Study Design



What were the results of the pediatric trial? Did they correlate with the adult data?

A total of 142 subjects were enrolled at seven study centers throughout the United States. Of the 142 subjects, 139 were evaluated for efficacy and all subjects were included in the safety analysis.

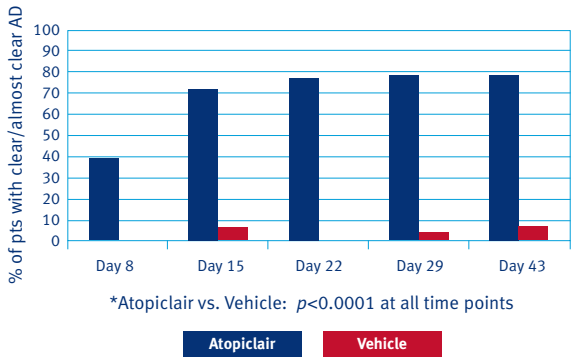
The outcomes of the pediatric study very closely mimic what was seen in the adult trial. The primary endpoint of this pediatric study was IGA at Day 22. A highly significant difference was found in the IGA scores at Day 22 between Atopiclair and vehicle treatment groups. By contrast, no treatment successes were reported in the vehicle group.

Secondary endpoints included IGA of atopic dermatitis at other time points, patient's/caregiver's assessment of pruritus (VAS score 1–100mm), EASI at all time points, onset of itch relief and duration of action, and the need for rescue medication in the event of a flare.

In 53 of the 69 patients enrolled in the Atopiclair arm, the IGA was either 1 or 0. That is, 77 percent of those who received Atopiclair at Day 22 were seen to have clear/almost clear atopic dermatitis. This number increased to 78.2 percent at Day 29 and remained stable until the end of the study. These are highly statistically significant data. In addition to the Day 22 IGA, the investigators looked at scores at Day 8 and at all other time points. Improvements in IGA scores were observed as early as Day 8, where 39.1 percent of subjects in the Atopiclair treatment group reached an IGA of "clear" or "almost clear."

Highly statistically significant improvement of the IGA scores for those patients randomized to Atopiclair is seen at all measurement periods of the trial **(Figure 2)**.

Figure 2. Investigator's Global Assessment of Atopic Dermatitis Treatment Successes ("Clear" or "Almost Clear" Ratings).



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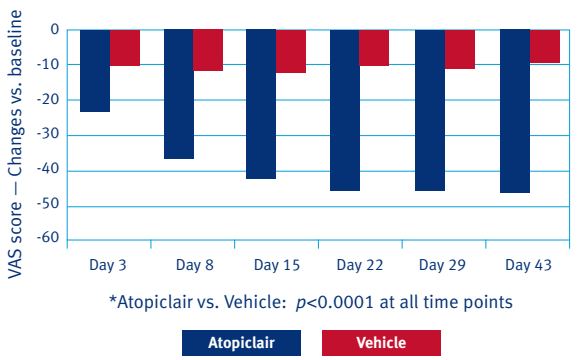
In the Atopiclair group, the assessment of the global response in terms of improvement by Day 8 was 60.8 percent improvement and by Day 43, 81.1 percent (for pediatric trials, FDA allows caregivers to answer on behalf of the child). In the group who received vehicle, the values did not improve more than 10 percent, so again a marked difference between study cohorts was noted. A highly statistically significant change in the subject and caregiver assessment of global response was reported in this pediatric trial.[1]

Figure 3. Assessment of Pruritus



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Were there any serious adverse events?

Adverse events were rare in this particular clinical trial. There was one adverse event in each arm of the study that was considered severe. One patient from the Atopiclair arm was hospitalized for a tonsillectomy (surgery had been scheduled prior to trial enrollment) and one from the vehicle arm was hospitalized for an asthma attack. According to trial protocol, both were reported as adverse events. No serious adverse event was related to the medication. Treatment discontinuation (permanent or temporary) as a result of an adverse event occurred in 9.9 percent of subjects treated with Atopiclair and 16 percent of those treated with vehicle (adverse events were similar in nature in both groups). Most adverse events, 91.3 percent, resolved without intervention during the study.[1]

Since itching is such a clinically significant problem with pediatric patients, what did the study show in regard to pruritus relief?

One of the outcome measures for which the investigators were particularly interested was the impact on itching. Unlike the vehicle arm, the Atopiclair arm shows sharp decreases in the VAS mean values from baseline to Day 43 **(Figure 3)**.

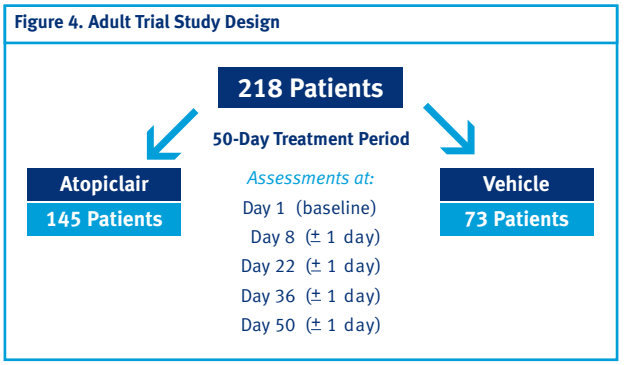
Itching remains one of the most troublesome components of atopic dermatitis management, particularly for pediatric patients because they do not have enough self control at very young ages to refrain from scratching their skin, often worsening their overall skin assessment. In the pediatric trial vehicle arm, even by Day 43, the subject and caregiver assessment showed only a one-percent overall improvement of control of itching. By comparison, for those randomized to the Atopiclair group, in terms of complete resolution of the itching, 27 percent felt that there was complete resolution of itching as early as Day 3. When we looked at this same parameter by Day 43, 65 percent of the Atopiclair subjects reported complete resolution of itching ($P<0.05$).

The study investigators also wanted to measure itch relief between each application. In the Atopiclair randomized group, by Day 8, the time of relief of the itch between applications was 201 minutes. The Atopiclair group by Day 43 had achieved 345 minutes between applications. By comparison, the itch relief for the vehicle group on Day 8 was 109 minutes between applications. And, by Day 43, the vehicle group showed very little if no improvement in itch relief by demonstrating only 112.9 minutes between applications ($P<0.05$). The statistically significant improvement outcome in the Atopiclair group is interesting to note, due to the fact that these children were not allowed to take antihistamines during the course of the study, which further emphasizes the longevity of control of itching.[1]

Was Atopiclair studied with adult patients previous to the study using infants and children? And, if so, what were the results?

A study encompassing adult patients was conducted using a multicenter, randomized, double-blind, vehicle control in multiple sites throughout the United States with enrollment beginning in November 2004 and completion in May 2005.[7] In this adult setting, 218 patients were enrolled in a 50-day treatment period, just slightly longer than the pediatric trial. The adult study used a 2:1 randomization (different than the pediatric trial) with twice as many patients enrolled in the Atopiclair arm as compared to the vehicle arm. The adult patients in the study were evaluated on Days 1 (baseline), 8, 22, 36, and 50, at which time the treatment was stopped. There were windows of 1 to 2 days for most of these visits **(Figure 4)**.

Figure 4. Adult Trial Study Design



To be eligible to enroll in the study, the adult patients had to be greater than 17 years of age and have atopic dermatitis that met the criteria for mild-to-moderate range. In addition, each patient had to have at least a 40-mm designation of itching on the visual analog scale (VAS) for the target lesion. The VAS is a linear-scale marking, entered by the patient, from 0 to 100mm. The VAS for itching is a validated method for assessing itch.[11] The patient marks on a line, from 0 to 100mm with 0mm being no itch and 100mm being the worst possible itch. The VAS is dated and initialed by the patient to validate the evaluation. The mean VAS scores for itch at baseline were 66.24±17.53mm in the vehicle group versus 60.28±16.88mm in the Atopiclair group (P=0.04). The target lesions were most commonly identified on the extremities, with 40 percent on the lower and 32 percent on the upper limbs.

The exclusion criteria for the adult patients were much the same as those set forth in the pediatric trial. Patients could not have any other skin condition, such as dermatomyositis, morphea, or psoriasis, that could interfere with the study. The duration of treatment for the adult trial was 50 days and a washout period of seven days if they had been on topical steroids or other agents that might have influence on their atopic dermatitis prior to enrollment.

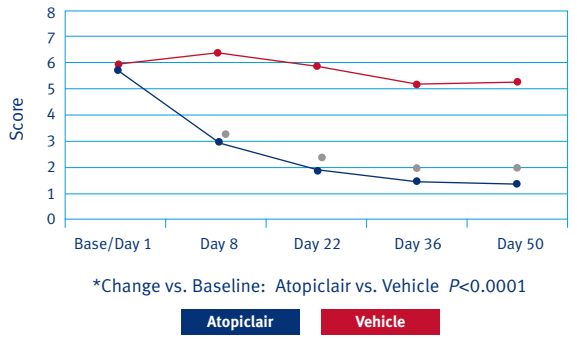
The Atopiclair and vehicle control were applied three times daily to the affected areas or the areas that might have become affected with atopic dermatitis, i.e., the antecubital fossa—a common area for atopic dermatitis. Subjects were told to apply Atopiclair or vehicle (blinded) on existing atopic dermatitis three times daily. In addition, they were told to apply the product three times daily on areas where they usually experience a flare, even if at enrollment there may have been no flare present.

The primary endpoint for the adult study was the EASI from baseline to Day 22. There were a number of secondary endpoints including EASI at all other time points, percentage of affected body area, itch score, the IGA of clinical response from baseline, the need for rescue medication (typically a topical steroid) in the event of a flare, and the patient's own assessment.

The results of the adult trial were dramatic. The assessment of EASI values at Day 22 compared with baseline showed no change in the vehicle group, in contrast with an appreciable improvement in the Atopiclair group. The mean value of treatment difference was -3.67 in favor of Atopiclair, with a 95-percent confidence interval. The difference between treatments was highly statistically significant (P<0.0001) **(Figure 5)**.[7]

There was a marked and very statistically significant difference in EASI between Atopiclair and vehicle at every time point. Interestingly, these data were replicated in the pediatric trial, which validated the results in the trial that involved infants and children. The adult trial demonstrated that there was superiority between Atopiclair's performance on the EASI score when compared to the vehicle.

Figure 5. Change in Eczema Area and Severity Index (EASI) Over Time



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In terms of itching, the adult trial demonstrated highly statistically significant results ($P<0.0001$). The statistical analysis performed on changes versus baseline showed a highly significant difference between treatments at all time points **(Figure 6)**. The mean VAS values of itch on target lesions decreased sharply from baseline throughout all time points in the Atopiclair group; whereas, only a slight decrease was observed in the vehicle group.[7]

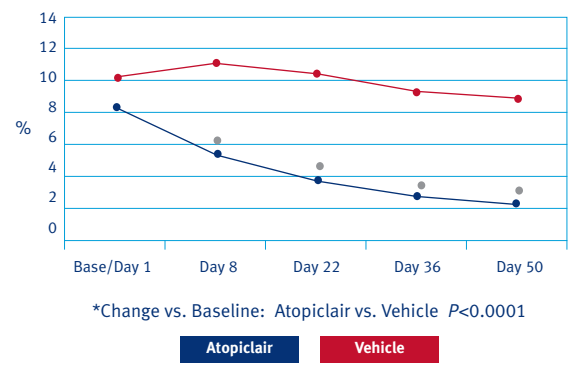
The assessment of body surface area in the adult trial as well as the IGA of clinical response from baseline showed a consistent improvement of the affected area in patients treated with Atopiclair. These values remained nearly unchanged throughout the study in patients treated with vehicle.[7]

The need for rescue medication paralleled much of the other responses in that far fewer patients randomized to Atopiclair required rescue medicine (which was a low-strength topical steroid) compared to those randomized to the vehicle group (6% vs. 40%, respectively). Also, 92 percent of the patients who received Atopiclair as part of this adult study said they would continue using it if they were allowed to do so.[7]

The incidence of treatment-related adverse events was low in both groups. During the study, 32 percent of the Atopiclair-treated and 26 percent of the vehicle-treated subjects experienced at least one adverse event. Adverse events were infrequent and comparable between the treatment groups. Generally, Atopiclair was well tolerated, with a safety profile comparable to that of the vehicle.[7]

The results of the adult study showed that Atopiclair is rapidly effective and safe as a nonsteroidal monotherapy in mild-to-moderate atopic dermatitis, showing that it may be useful as a topical steroid-sparing agent.[7]

Figure 6. Change in Itch Target Lesion (VAS) Score Over Time



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Were the exclusions for the pediatric trial similar to those in the adult trial?

The exclusion criteria for the pediatric trial very closely matched those of the adult trial. Individuals were not allowed to enroll in the study if they had active skin infection at the initial visit. After skin infections were cleared, subjects were allowed to enroll in the study. Any female adolescent of childbearing age (achievement of menses) was not allowed to enroll in the study.

Other exclusion criteria included subjects with type 1 diabetes; a known allergy to any Atopiclair ingredient; and any interfering condition, such as psoriasis, dermatomyositis, or another skin condition that might hinder interpretation of data.[1]

What else can we do, as dermatologists, for pediatric patients as well as adult patients to help ensure compliance with a regimen for managing atopic dermatitis?

Education is key. Tell your patients and/or their caregivers how many times each day they should use each product. Separate the products into categories (e.g., regular moisturizer, barrier repair cream, topical steroid, and calcineurin inhibitor). Each has its own function. Explain exactly what to do with each. Lay out their schedules and expectations.

Prevention of flares of atopic dermatitis involves avoiding and/or reducing the identifiable triggers and maintaining a good skin care regimen. A good prevention program should be tailored to each patient. Explain to the patient, whose disease is exacerbated by dust mites (for example), that he or she can employ several measures to decrease household dust-mite burden, including adequate household ventilation, mattress covers, pillow covers, avoiding wall-to-wall carpeting, removing dust with a damp sponge, vacuuming floors and upholstery at least once a week, washing linens in hot water every 7 to 10 days, and decreasing indoor humidity levels with air conditioning. In the winter, patients should be advised to increase emollient use.

Patients may not know that clothing made of synthetic fibers and wool should be avoided to prevent flares of itching. Soft clothing with fabrics such as cotton should be recommended. Mild soaps with a neutral pH and minimal defatting capabilities should be used for bathing in all patients with atopic dermatitis, and patients should bathe in warm water once daily for 5 to 10 minutes, pat dry, and immediately apply emollients. Finally, nails should be trimmed to decrease abrasions to skin.

Children with atopic dermatitis experience the same, intense, unbearable itching as adults. But, unlike adults, children cannot keep themselves from scratching (which makes the itch more intense). The itch becomes more intense at night, potentially interrupting sleep. This may be because there are fewer distractions at night, and the itch becomes more noticeable.

Emotionally, a child is forced to cope with a change in his or her appearance (flares generally occur on the face, arms, and legs). Children of color sometimes show a follicular pattern of disease that can lead to a rough-appearing surface of the skin. Additionally, the inflammation caused by the dermatitis can result in postinflammatory hypo- or hyperpigmentation, which can last for many months.[12]

How often do children with atopic dermatitis, especially those with severe disease, develop behavioral and emotional problems from the very pruritic and disabling aspects of the condition?

Very few controlled studies have examined the prevalence and types of psychological disturbance or the problems experienced by parents of these patients. Investigators have studied psychological problems in children aged 5 to 15 years with all degrees of atopic dermatitis.

In one study, 30 pediatric patients with atopic eczema and a comparison group of 30 age-matched children with minor skin problems were evaluated by a child psychiatrist using a popular, standard questionnaire (Rutter A2 Scale). Parental mental distress and family social support were also assessed. Psychological disturbance was found in 50 percent of children with eczema versus 27 percent of controls. The rate of psychological disturbance was 53 percent in children with moderate eczema and 80 percent in those with severe eczema. The majority (80%) of atopic children with psychological problems had emotional disorders, while 20 percent had conduct problems. No increase in hyperactivity disorders was seen in the atopic group compared with controls. The degree of maternal emotional distress and family social support was similar in the two groups.[13]

Other conditions, such as leukemia, diabetes, and epilepsy many times require psychological assistance. In this same fashion, attention to the emotional and behavioral problems in atopic patients may lead to improvement in the skin disease. For particularly severe cases, it may help both the patient and caregiver to enlist the help of psychological management.[13]

What is the current thinking regarding the theory that children with atopic dermatitis have hypersensory sensitivity?

A recent study published in the October issue of the *Journal of the American Academy of Dermatology* studied Short Sensory Profile, which covers a range of sensory modalities including tactile sensitivity, taste, and smell. The study enrolled 53 patients with atopic dermatitis and 61 healthy controls, aged 3 to 10 years. The study reported that children with atopic dermatitis have significantly higher sensory sensitivity for most modalities, especially tactile sensations. Understanding the special needs and behavioral characteristics of atopic dermatitis patients can lead to a more positive intervention program for children with atopic dermatitis. Certainly, the quality of life for pediatric atopic dermatitis patients is compromised.[14]

In fact, another recent study published in *Pediatrics* last September found that atopic dermatitis had a greater impact on family quality of life than type 1 diabetes. Across all ages and ethnic groups, the researchers found a steady increase in the number of doctor and hospital visits for atopic dermatitis. Patients between 2 and 5 years old were more likely than older or younger children to be seen for atopic dermatitis (odds ratio 2.4 compared with children ages 11 to 18 years, p=0.001). Compared with Caucasian patients, the odds ratio was 1.9 for Hispanic children (p=0.02), 2.2 for African-American children (p=0.001), and 3.1 for Asian children (p=0.001).[15]

How do you explain barrier dysfunction and repair to patients and caregivers?

When you are dealing with pediatric atopic dermatitis patients and their caregivers, it is important for them to visualize the problem. Obviously illustrated charts help, but think of something more at the level of the child, and use a white wiffleball. Explain to the patient and parents that the skin has little holes, just like the ball. Atopiclair helps them to seal those holes. The holes never really go away. The job is an ongoing one, so the holes must be constantly sealed. Use the example of a little bit of Vaseline® to seal chapped lips. The lips feel immediately better with the application of a thin film of Vaseline and the lips then heal quickly. Vaseline is not a medicine, but, rather, like a device. The same is true with Atopiclair. By sealing those imperceptible holes that let the water out and allow allergic trigger factors to invade the skin, the skin is allowed to heal. This visual example can help parents and patients understand the principles of treatment and the role that they need to play in determining a successful outcome.

In providing advice for when to stop using topical steroids for atopic dermatitis, request that parents feel the skin for small bumps that represent the spongiotic dermatitis. If the bumps are imperceptible, then they can stop the topical steroid and just use the barrier repair cream or emollient. Touch usually works better than visual examination because patients sometimes see pigmentary disparity and may construe that as eczema. Color discrepancies that come and go over long periods of time represent changes in the skin that relate to pigmentary increases or decreases. As patients return for follow-up, make adaptations for changes and seasonal variation. Work very closely with the parents to help with ongoing education.

Educating patients and their caregivers is important, but how do dermatologists educate other healthcare providers regarding the understanding of barrier repair and the importance of a proven, nonsteroidal solution?

The basic science of barrier defending is new to many physicians. This is an educational challenge. The healthcare community is aware of the need for steroid-free maintenance treatments for atopic dermatitis. Atopiclair has been studied in double-blind, multi-center, randomized trials in both pediatric and adult patients with atopic dermatitis. In addition, the pediatric trial has replicated many of the favorable outcomes of the adult trial with statistically significant results.

How do you manage atopic dermatitis patients who tell you that anything they apply to their skin burns?

For some patients, especially pediatric patients, everything they put on their atopic dermatitis feels as if it burns the skin, even Atopiclair. For these patients, helpful advice would be to use olive oil first. Use it as a spray for easy application to any body area, including the antecubital fossa. Once the olive oil has formed a thin coating on the skin, apply the Atopiclair. If the barrier is a little bit less dysfunctional or broken, patients are able to tolerate barrier creams without any burning sensation. Remember that lotions can burn, sting, and even dry out skin. These patients should stay away from lotions that contain more water and may lead to greater impediment of skin hydration from evaporative losses.

Roundtable Executive Summary

For decades, topical steroids have been a mainstay of therapy in patients with atopic dermatitis, but their chronic use or even short-term use can be associated with adverse effects, including irreversible striae and skin atrophy and, rarely, inhibition of the hypothalamic-pituitary-adrenal axis. In addition, patients or parents and healthcare providers have manifested concerns about the use of topical steroids.[16] Concerns about long-term safety with their use have been raised.[16]

A roundtable advisory meeting was held to facilitate peer discussion regarding a recently published trial that evaluated the efficacy and safety of a nonsteroidal cream, Atopiclair, in infants and children with mild-to-moderate atopic dermatitis.

The results of this study demonstrated that Atopiclair cream is rapidly effective and safe as nonsteroidal monotherapy in mild-to-moderate atopic dermatitis and that it may be useful as a topical steroid-sparing agent.[1] The study also demonstrated significant early improvement of itching, with some subjects experiencing complete resolution of itching as early as Day 3.

Atopiclair has demonstrated rapid, highly statistically significant efficacy and safety in the pediatric trial, and the positive results of an adult trial mirrored the success of the pediatric trial, also showing that Atopiclair is rapidly effective and safe as nonsteroidal monotherapy in mild-to-moderate atopic dermatitis.

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