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TACROLIMUS OINTMENT VERSUS PIMECROLMUS CREAM IN PATIENTS WITH ATOPIC DERMATITIS INVOLVING THE HEAD AND/OR NECK
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Objective: To compare the efficacy and safety of tacrolimus ointment and pimecrolimus cream in adults and children with atopic dermatitis (AD) involving the head and/or neck.

Methods: Three randomized, investigator-blinded, 6-week, multicenter studies were conducted using identical study design. Patients were randomized (1:1) to tacrolimus ointment or pimecrolimus cream. All adult patients (at least 16 years) and pediatric patients (2–15 years) with moderate AD received tacrolimus ointment 0.1% or pimecrolimus cream 1%. Head and neck data were analyzed for efficacy. Safety endpoints were the overall incidences of all adverse events reported/observed in all treatment areas.

Results: Of 1060 patients enrolled in these 3 studies, 710 had head and/or neck involvement at baseline. In the combined analysis, there was a 57% improvement in the Eczema Area and Severity Index (EASI) and a 78% improvement in the Investigator’s Global Assessment (IGA) for patients treated with tacrolimus ointment compared with 27% for pimecrolimus cream. Head and neck data were analyzed for efficacy. Safety endpoints were the overall incidences of all adverse events reported/observed in all treatment areas.

Conclusion: Tacrolimus ointment is superior to pimecrolimus cream in the treatment of AD in the head and neck region, with a similar incidence of adverse events.

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THE PALMITOLEYLANOLAMIDE FAMILY: A NEW TREATMENT CHOICE FOR ATOPIC DERMATITIS
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A number of immunoregulatory abnormalities are known to play a role in the pathogenesis of atopic dermatitis (AD), including increased IgE synthesis,1 increased histamine release from histinophils,2 impaired delayed-type hypersensitivity response,3 and elevated levels of cytokines.4–6 For example, overproduction of interleukin 4 (IL-4) in AD patients is thought to be critical in AD pathogenesis.1 The cornerstone of AD treatment has been corticosteroids because corticosteroid therapy provides an effective way to combat the overactive inflammatory system. However, corticosteroids can have unacceptable side effects and are used on a short-term basis and intermittently on a long-term basis. These side effects are especially of concern in children, who represent the majority of the AD patient population. Thus, a nonsteroidal anti-inflammatory treatment option for AD patients would be a great benefit. PEA, also known as N-palmitoylethanolamide, is an endogenous anti-inflammatory compound found in skin and other tissues and would provide an alternative treatment to corticosteroid treatment of AD. PEA accumulates during inflammation, and several studies have reported PEA-induced anti-inflammatory and analgesic effects in clinics and animals.7–9 In addition, PEA is known to control the inflammation and proliferation of tumor cells,10 to down-regulate IL-4 in human monocytes,11 and to inhibit cycoxygenase activity and free radical production in a rat model of carrageenan-induced acute paw inflammation.12 The available animal data have clearly distinguished PEA from anti-inflammatory agents such as nonsteroidal anti-inflammatory drugs and corticosteroids; however, its precise mechanism of action is unknown. PEA is currently undergoing phase II clinical trials for the treatment of chronic lumbar sciatic pain and multiple sclerosis.13 In addition, PEA has been the subject of several AD pilot studies. Promising preliminary results from the AD studies indicate that PEA is an important compound and should be considered for the treatment of AD patients (unpublished data).

References

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THE PHARMACOLOGY AND PHARMACOKINETICS OF CLOCORTOLONE PIVALATE CREAM 0.1%
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Clocortolone pivalate cream 0.1% (9-chloro-6-fluoro-11β,16α-methylpregnan-1,4-dien-3,20-dione-21-pivalate) is a mid-potency corticosteroid that is unique in having a single chlorine and single fluorine molecule in its structure. Human pharmacology testing indicated that clocortolone pivalate would be well tolerated and safe to use for therapy. Drazke sensitization studies, both in the absence and presence of ultraviolet light, showed no evidence for contact sensitization and application of clocortolone pivalate to both forearms after removal of the stratum corneum and irradiation with Woods light gave no evidence for photocotoxicity. After application of clocortolone pivalate to the skin for 21 days, the potential to cause irritation was very low. Permeation studies, both in vitro and in vivo, in normal and inflamed human skin, showed that clocortolone concentration in the epidermis of inflamed skin was 19 times greater than in normal skin in the in vitro studies and 178 times greater in the in vivo studies.

Measurement of urinary 17-ketosteroids and serum cortisol levels during a 21-day study in which 50 g of clocortolone pivalate cream was applied, under occlusion, twice daily to 10 human volunteers, showed that there was no adrenal suppression. Because the cream has shown good efficiency in treating various dermatoses, it is concluded that after topical application, clocortolone is readily bioavailable for local activity in the skin, but has little potential to enter the systemic circulation.

Studies in rats have shown that after topical application most of the clocortolone remains at the site of application, with only 2% reaching the deep layers of the stratum corneum. After oral administration of clocortolone pivalate to rats, 20% was excreted in the urine and 67% in the feces.

These studies will be described in detail and will show that the unique structure of clocortolone pivalate gives it a pharmacological profile that makes it eminently suitable for human use.

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