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Molecule | Commercial Names
---|---
fluticasone propionate | Cutivate®
alefacept | Amevive™
valcyclovir | Valtrex®
imiquimod | Aldara™
mometasone furoate | Eloxon/Elocom®
hydrocortisone valerate | Westcort®
fluocinonide | Lidex®
triamcinolone | Kenalog®
betamethasone valerate | Valisone®
clobetasone butyrate | Eumovate®
pimecrolimus | Elidel®
tacrolimus | Protopic®

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betamethasone valerate | Valisone®
clobetasone butyrate | Eumovate®
pimecrolimus | Elidel®
tacrolimus | Protopic®
This issue of Focus on Dermatology is different from the others. This issue brings you information on Dermatology Update, a leading forum for the sharing and learning about new drugs and exciting new therapeutic approaches in the field of dermatology. Dermatology Update held its 20th meeting in Vancouver, BC October 14-16th, 2004. It combined workshops and plenary sessions led by Canadian dermatologists and international speakers. This issue of Focus on Dermatology brings you some exciting reports from those workshops and introduces you to two new drugs recently approved in Canada, Amevive and Cutivate.

The reports have been written by dermatologists who presented at the conference and who have a strong interest in the subject areas. The topics were chosen by the Focus on Dermatology Editorial Board who believed that the information in these workshops needed to be shared with their colleagues. In particular, they expressed their concern regarding therapeutic treatments and patient’s quality of life. As you will see in many of the articles, dermatological diseases have significant effects on patient’s quality of life. The message from many of the presenters at the conference was that therapy should improve the patient’s quality of life while minimizing side effects. Appropriate management of psoriasis, atopic dermatitis and acne can significantly mitigate impact on a patient’s quality of life and potentially reduce the cost on the healthcare system.

Amevive is a recently approved biologic agent for the treatment of psoriasis. It offers dermatologists another option for treating moderate to severe psoriasis along with their current therapies such as UV-B, cyclosporine and methotrexate.

Cutivate is a recently approved potent topical corticosteroid for the treatment of atopic dermatitis. Cutivate has been available in the USA and the UK for over 10 years and has had few instances of adverse events. It offers general practitioners and dermatologists a new tool for treating moderate to severe atopic dermatitis. The Canadian Cutivate Advisory Board recently released the following consensus statement on the usage of Cutivate in Canada:

Cutivate is a new, potent, topical corticosteroid shown to be safe and effective for the treatment, over a four week period, of moderate to severe atopic dermatitis (level 1 evidence). Skin thinning was shown to be no worse than placebo while demonstrating limited potential of systemic effect in clinical studies (level 1 evidence). Cutivate has further been clinically demonstrated as safe for use on children over 3 months of age. When used twice weekly, Cutivate prevents or controls AD and offers effective long-term maintenance of AD (level 1 evidence). Intermittent use of Cutivate is an alternative product for long term control of atopic dermatitis.

Future issues of Focus on Dermatology will continue to contain a blend of information on therapeutic options for the treatment of dermatological diseases including abstracts and meeting reports. We look forward to continuing our dialogue with you.

Bonnie Kuehl PhD
Long-Term Management of Atopic Dermatitis

John Berth-Jones MD FRCP, Consultant Dermatologist, University Hospitals Coventry and Warwickshire, Coventry, UK

Atopic eczema or atopic dermatitis (AD) is a common chronic inflammatory, relapsing, skin condition for which there is no cure. The next best approach is a treatment strategy aimed at disease remission; however, no agreement exists on the best treatment plan for the long term treatment of moderate to severe AD. Despite the development of non-steroidal, anti-inflammatory treatments, topical corticosteroids remain the cornerstone of therapy for AD. A recent comprehensive systematic review found that maintenance regimens use one of two approaches: either a potent topical corticosteroid followed by a lower potency regimen or a short course of topical corticosteroid followed by a maintenance regimen of emollients. Concerns have been raised about the prolonged use of low potency topical corticosteroids, and, although treatment with emollient is safe, its efficacy as a maintenance treatment remains limited. Many patients use a maintenance treatment of emollient combined with intermittent topical corticosteroid. This approach was investigated recently in a small scale study, which showed that remission of atopic dermatitis can be maintained with daily emollient plus fluticasone propionate applied twice weekly to areas of the skin that had healed but were prone to relapse.

Fluticasone propionate (FP) is a potent topical corticosteroid which has high topical anti-inflammatory effects and a low potential to cause adverse effects because of low systemic absorption and rapid metabolism. Therefore, FP has a high benefit-risk ratio which is advantageous in a long term treatment strategy. This trial aimed to evaluate further the use of FP twice weekly as part of an emollient based maintenance regimen in patients with moderate to severe AD. The 295 patients enrolled in the maintenance phase of the study, twice as many patients were in remission after 16 weeks with twice weekly application of FP plus emollient versus emollient alone, following the initial stabilization of their condition with twice daily FP.

By preventing recurrent relapses of AD and therefore reducing the need for acute intensive short courses of daily topical corticosteroid therapy, this twice weekly FP maintenance regimen may have steroid sparing potential in patients with recurrent disease. In addition, by maintaining remission, application of FP will be limited mainly to healed sites, which are less permeable than inflamed lesions, and so the overall exposure to topical corticosteroids will be reduced. Little difference was found between once- and twice-daily FP treatment in the initial acute stabilization phase and this did not affect the risk of relapse in the maintenance phase. Therefore, to minimize steroid exposure, patients could start the stabilization period on a once daily FP therapy.

These results support the use of FP in a maintenance strategy. Whether or not this maintenance strategy can be applied to other topical corticosteroids remains to be established. The reduction in risk of relapse among the FP-treated subjects with AD may translate into a significant reduction in the national burden of this disease by considering AD as a skin disease that affects many children and adults. Moreover, there is the potential for a significant improvement in quality of life among subjects with AD.

Psoriasis: Therapy Choices

Charles Lynde MD, FRCPC, Assistant Professor University of Toronto and Lynderm Research Inc. Markham, Ontario.

It has been over ten years since the last significant advancement in the treatment of psoriasis; a disorder that we know has a very negative impact on our patients. There is no long term case with the recent approval of alefacept (Ameluz®).

Psoriasis is immune-mediated disorder that affects about 2.5% of the world’s population and approximately one million Canadians. The onset is usually between the ages of 10 and 40 years and is more prevalent in higher latitudes and in Caucasians than in any other race. The susceptibility to psoriasis is inherited, but environmental factors, stress and infections may determine disease onset and severity.

The literature has shown the negative effects that psoriasis has on the quality of life of patients. Rapp et al (1999) showed that patients with psoriasis had reductions in their physical and mental functioning comparable with that seen in congestive heart failure, cancer, arthritis and diabetes and depression. In 1998, a telephone survey of 6194 psoriasis sufferers reported that psoriasis had a negative impact on 79% of their lives, 40% felt frustrated with the ineffectiveness of their current therapies and 32% reported that treatment was not aggressive enough.

Current treatment of mild psoriasis is based on topical regimens such as tar, corticosteroids and vitamin D derivatives. For patients with moderate to severe disease, however, topical therapy is insufficient. In patients with moderate to severe psoriasis, more advanced therapies are often required. Advanced treatments in the past included ultraviolet (UV)-B light, psoralen plus UVA (PUVA) acitretin, methotrexate, cyclosporine and other immunosuppressive drugs in selected cases. These treatments have, until now, been the treatments of choice by default, but biologics tend to be more precise and specific in their effect by targeting various cytokine pathways.

To a vast amount of research, highly specific biologics that act on specific cell receptor pathways have been targeted. The targeted nature of these medications has led to side effects that are much lower than those of traditional advanced therapies. We have also found that biologics, with mechanisms that reduce T cells in skin lesions can provide our patients with remissions.

A recent American Academy of Dermatology consensus statement as well as a paper recently published in the Journal of Cutaneous Medicine and Surgery recommended that biologic agents be considered first line for moderate to severe psoriasis along with the more traditional advanced therapies. I have had the opportunity to use most of the biologic agents over the past few years. From this first hand experience, I have seen the incredible impact that these medications can have on the quality of life of our patients. They are truly a highly significant advance in the treatment of our patients. This new era of advanced therapies have highly specific biologic agents, which rebalance the immune system, was recently highlighted by the approval of alefacept, the only biologic currently approved for psoriasis in Canada.
Developing an Integrated Acne Severity Assessment Tool (ASSET)

Jerry Tan MD FRCP, Adjunct Professor
University of Windsor, Windsor, Ontario

At the recent Dermatology Update meeting held in Vancouver, BC an acne workshop focused on initiating the development of an assessment system for acne severity. This system would integrate the severity of active lesions, other clinical elements (lesional type / extent; scarring) and those determined by determining the relative weighting of the physician-rated lesions, presence or absence of scarring, and a psychometric score incorporating 3 relevant factors: extent and type of active acne lesions, presence or absence of scars and psychosocial impact. While there are more than 25 classification systems for grading acne severity, none exist that integrate the presence of scars or psychosocial impact. It is anticipated that such an evaluation system would be relevant, practical and useful in overall clinical assessment of acne and in guiding management.

The workshop, sponsored by Berlex, manufacturers of Diane-35™, was attended by Canadian dermatologists with an interest in acne research. Presentations were by Dr. Jerry Tan (University of Western Ontario) on clinical findings from the Canadian Acne Epidemiology Study and Professor Andrew Finlay (University of Wales) on quality of life measurements in dermatology.

Acne grading systems in clinical practice will be useful if based on practicality, simplicity of use, and relevance to management. One such system developed in Leeds is based on photographic templates of increasing severity: 15 for the face, and 8 each for the back and chest. Another system, intuitively appealing and of clinical relevance, is the global assessment score mandated by the FDA (grades of clear, almost clear, mild, moderate, severe and extremely severe). Dr. Tan presented data from the Canadian Acne Epidemiological Project on more than 1000 patients demonstrating that these two systems were well correlated; however, shortcomings of the Leeds system were found and included poor discrimination of the almost clear and mild categories and an over-representation of the severe spectrum. He reported that current efforts are underway to update the photographic template system based on the global assessment definitions.

The presence of acne scarring was considered to be an important determinant of overall acne severity. Dr. Tan reported that facial scarring was observed in over 85% of patients in the Canadian cohort. Patients with a minimum threshold of mild scarring were more likely to be aware of the presence of scars than those with lower scar grades.

Dr. Finlay spoke on the increasing role of psychometric measures (quality of life scales) in the study of skin disease. The measurement of psychosocial impact of disease sufferers has, until recently, been a neglected component of the clinical paradigm in dermatology such as the Disease Life Quality Index (DLQI) and specific scales such as the Cardiff Acne Disability Index (CADI), both of which Dr. Finlay co-developed, are used to measure psychosocial impact. While most QoL measures are based on responses to multiple questions (DLQI contains 10 items; CADI 5 questions), these may be impractical in daily clinical practice. Ideally, a simple, rapidly-completed 1-2 item questionnaire would provide greater practical utility. Current efforts are underway to determine which individual items within the CADI demonstrate the highest correlation with the overall score.

The Vancouver workshop successfully initiated the development of ASSET, an integrated acne severity assessment tool incorporating 3 relevant factors: extent and type of active acne lesions, presence or absence of scarring, and a psychometric score reflecting psychosocial impact. Future research will include (1) determining the relative weighting of the physician-rated elements (lesional type / extent; scarring) and those determined by patient responses (quality of life scores); and (2) validating the new assessment tool in clinical practice.

Valacyclovir in the Treatment and Prevention of Herpes Infections

Stephen K. Tyring, MD, PhD, MBA,
University of Texas Health Science Center, Houston, Texas

Valacyclovir is the prodrug of acyclovir; when taken orally it achieves blood levels of acyclovir that are equivalent to receiving intravenous acyclovir. Valacyclovir is indicated for the episodic therapy of herpes labialis at 2g BID for one day and for the episodic therapy of genital herpes at 500mg BID for three days.

It is used to suppress recurrent genital herpes at 500mg daily, which results in a 90% reduction in both clinical outbreaks and asymptomatic viral shedding. This observation led to a recent study demonstrating that taking valacyclovir 500mg daily by a person with genital herpes could reduce transmission to a seronegative partner by 77%. This study was the first demonstration of an antiviral drug reducing the transmission of a sexually transmitted disease.

Valacyclovir is also approved for the therapy of acute herpes zoster at 1g TID for seven days, which is more effective at reducing zoster associated pain than is acyclovir 800mg five times daily. Recently valacyclovir at 1g TID for seven days combined with gabapentin at escalating doses over one to two months was found to reduce (relative to valacyclovir monotherapy) the incidence of zoster associated pain by 80% at six months following the development of acute zoster.

When valacyclovir is taken episodically for therapy of herpes labialis, genital herpes or herpes zoster or is used daily to suppress genital herpes, it is equally safe as placebo. Likewise, valacyclovir is used safely and effectively to treat herpes labialis, genital herpes and herpes zoster in immunocompromised patients.

In conclusion, valacyclovir is safe and effective for treatment of herpes labialis, herpes genitalis and herpes zoster. It is the only antiviral drug proven to reduce transmission of a sexually transmitted disease. When combined with gabapentin for therapy of acute herpes zoster, it is very effective at preventing zoster associated pain.
Imiquimod (Aldara™) is a topical cream that is indicated for the treatment of actinic keratosis and external anogenital warts. It acts through the stimulation of both the body’s innate immunity and cell mediated immunity.

Actinic keratoses present on sun damaged skin as ill defined slightly scaly erythematous to hyperpigmented papules. They are most commonly located on the face, arms and hands. Imiquimod has demonstrated excellent efficacy in the treatment of actinic keratoses. In two multicentre randomized placebo-controlled parallel-group studies, imiquimod therapy resulted in a median reduction in the number of actinic keratoses by 83%. In a similar study that examined clinical and histological effectiveness, imiquimod resulted in complete clearance in 57% of patients and >75% clearance in 72% of patients. The majority of patients treated with imiquimod develop signs of inflammation at the treatment site. Erythema, flaking and crusting are the most common side effects. Patients, however, do not experience a significant difference in pain or stinging at the treatment site and only 3% of patients actually discontinued treatment because of side effects.

For the treatment of actinic keratoses, imiquimod is applied to the affected area on two nonconsecutive days per week for 16 weeks. Patients are allowed to take breaks from treatment if they feel it necessary because of side effects.

External anogenital warts, condyloma acuminate, are present in female patients as either small or large verrucous papules or plaques on vulvar or perianal skin. In male patients, similar lesions may develop on the penis, scrotum, perianal area and surrounding skin. Imiquimod is very efficacious in the treatment of external condyloma acuminate. In a pivotal randomized placebo-controlled study, imiquimod demonstrated complete clearance of warts in 77% of female subjects and 40% of male patients. Even in those patients who did not clear, a reduction in total wart area >50% was demonstrated in 85% of women and 70% of men. The average time to total wart clearance was only 8 weeks for women and 12 weeks for men. As with actinic keratoses, local inflammation is an expected side effect, with the majority of treated patients experiencing erythema.

Aldara™ should be applied on 3 nonconsecutive nights per week at bedtime, for a maximum of 16 weeks. The cream should be washed off in the morning and sexual contact should be avoided while the cream is on the skin. Although treatment may continue for up to 16 weeks, treatment should be discontinued earlier if the warts clear completely. Additionally, breaks in treatment because of inflammation are permitted.
**Amevive™ Product Information**

**Indication**
For the treatment of patients with moderate to severe chronic plaque psoriasis who are candidates for phototherapy or systemic therapy.

**Dosing**
Once weekly IM injections for 12 weeks, with a minimum 12 week treatment free period

**Treatment Length**
12 week intermittent dosing (ie 12 weeks on and 12 weeks off before a second course)

**Expected Time to Response**
Initial response at 6-8 weeks with maximal response at 8 weeks after last dose (week 20)

**Rebound Effect**
None observed

**Safety**
In clinical trials no difference in side effect profile was observed between Amevive™ and placebo.

**Concerns or Contraindications**
Patients with a known hypersensitivity to Amevive™

*This is abbreviated prescribing information, full product monographs are available by contacting the respective companies directly.*

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**Cutivate® Product Information**

**Indication**
For the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Proven efficacy for treating mild to severe atopic dermatitis.

**Dosing**
Apply a thin film of Cutivate® Cream to the affected areas once or twice daily until clear.

**Safety**
Low potential for HPA-Axis suppression or skin atrophy.

**Contraindications**
Not indicated for patients with a hypersensitivity to any of the components. Contraindicated in the treatment of rosacea, acne vulgaris, periapical dermatitis, primary cutaneous viral infections, perianal and genital pruritus, primary infected skin lesions caused by infection with fungi or bacteria.

*This is abbreviated prescribing information, full product monographs are available by contacting the respective companies directly.*
Abstracts reviewed in this issue


Alefacept is a novel biologic agent that selectively targets the memory T-cell population involved in the pathogenesis of psoriasis. Alefacept, administered by intramuscular (IM) or intravenous (IV) bolus injection, is safe and efficacious and improves quality of life in a broad spectrum of psoriasis patients. Disease remissions last approximately 7 months in responders following either IM or IV administration without further treatment. In clinical studies, treatment of patients with psoriasis with up to six courses of alefacept demonstrates the following: no evidence of an increased risk for infection or malignancy; no correlation between rates of infection, malignancy, and circulating CD4+/CD8+ T-cell counts; and low immunogenicity. A preliminary study evaluating the use of alefacept for the treatment of active psoriatic arthritis parallels the psoriasis experience and supports the premise of targeting T cells as an intervention for this disease. Research continues to examine the use of alefacept in combination with other systemic psoriasis therapies and phototherapy and its potential as a treatment for other T-cell-mediated diseases, such as psoriatic arthritis, alopecia areata, and rheumatoid arthritis.
Fluticasone propionate (FP) 0.05% (Cutivate®) cream is a novel corticosteroid used for the treatment of corticosteroid-responsive dermatoses. To date there are no published data concerning its effect on cutaneous atrophy. This randomized, double-blind study of 40 volunteer subjects was performed to investigate the kinetics of skin thinning induced by topical 0.05% FP cream vs. placebo after once-daily application for 2-8 weeks. The results of this study showed no significant effect on the skin thickness of subjects after 8 weeks’ treatment with 0.05% FP cream compared with placebo.

The study by Dykes PJ et al. showing no skin atrophy on the forearm of 40 volunteer subjects is important information for the clinician. To date the potential atrophogenic effects of potent topical corticosteroids has been a major consideration when deciding on prolonged use of these drugs. Most studies investigating the atrophogenic effect of topical steroids have used twice a day applications; it is therefore difficult to compare results with this study which used the drug daily. Regardless of this, it is comforting to know that at 8 weeks there is no atrophy seen on ultrasound, clinically or histologically when Fluticasone propionate 0.05% cream is used daily which has been shown to be clinically as effective as twice a day use. (Commentary by Dr. Thomas)

The cosmetic and physicochemical properties of six topical corticosteroid creams were evaluated and compared. The following creams were provided in blinded tubes: Elocon, Westcort, Lidex, Kenalog, Valisone, and Cutivate. The following properties were evaluated in vitro: stiffness (hardness), grittiness, color, odor, homogeneity (phase separation), pH, weight loss, and tackiness (stickiness). Samples of the creams were evaluated by light microscopy and scanning electron microscopy to identify particle and droplet distribution, particulate contamination, and microscopic homogeneity of the products. Cutivate ranked number 1 in each category and received the best overall score for each of the cosmetic and physicochemical properties evaluated. The cosmetic and physicochemical properties of Elocon, Westcort, Lidex, and Kenalog were found to be similar to one another with regard to overall score but inferior to Cutivate. Valisone was also good with regard to overall score but was ranked less acceptable due to a strong odor.

Patient compliance is important in the treatment of dermatological diseases, and can be influenced by the cosmetic acceptability of products. In this simple evaluation of cosmetic and physical chemical properties, no patients were involved, which is certainly unusual. It is also unclear whether the evaluations that are subjective for colour, odor and stiffness/spreadability are standardized accepted methods for in vitro determination of such properties. Certainly the evaluation of the pH, phase separation, weight loss and microscopic evaluation for homogeneity are well established methods. Considering these well established methods and excluding the rest, evidence shows that Cutivate ranks number one compared to the other topical corticosteroids. (Commentary by Dr. Vender)
4. Can Topical Corticosteroids Prevent the Relapse of Atopic Dermatitis?

Kuehl, B. and Lynde, C. Poster Presented at Dermatology Update October 2004, Vancouver BC.

Introduction: There is currently no generally accepted remedy or single treatment that can cure AD. Repeated treatment cycles are often necessary to achieve a stable state where flare-ups are controlled and their number reduced. Individual treatment for a patient is dependent on factors such as disease severity, age, potential compliance problems, efficacy, safety data and treatment costs. Therapies should offer patients sufficient clinical and subjective efficacy with a treatment modality that will encourage compliance, leading to an improvement in their quality of life. To prevent and reduce flares, long-term therapy regimens must be an ongoing daily occurrence with the use of emollients and then prescription medications being used to prevent and/or treat flare-ups. Methods: The present literature was analyzed to understand the current therapy options for long-term management of AD. The literature was examined following a search of MEDLINE and EMBASE databases. Search criteria included all articles on AD from January 1, 1995 to the present, published in English with human subjects including reviews, reports, and meta-analyses. Two different long-term maintenance therapy options were apparent during the review of the literature, one using topical corticosteroids and the other a combination of topical immunomodulators and topical corticosteroids. Discussion: Topical corticosteroids are widely prescribed for the treatment of AD and are considered to be the mainstay of AD therapy. They have been proven to be safe and efficacious in randomized, controlled trials for short-term (2 to 4 weeks) continuous use. The new TIMs, tacrolimus and pimecrolimus, have also been proven to be safe and efficacious in randomized, controlled trials for the short to medium term (6 months to 1 year) treatment of AD, and especially in the prevention of progression to flares. Randomized controlled clinical studies demonstrate that two long-term treatment options are viable for managing AD:

i) Fluticasone propionate twice weekly in addition to daily emollients decreases average time to relapse from 5-6 weeks to >16 weeks. Fluticasone propionate twice weekly was well tolerated by patients for up to 24 weeks with no reported incidence of skin atrophy or skin thinning. More studies are needed to evaluate the efficacy of other topical corticosteroids in preventing flares.

ii) Pimecrolimus twice daily in addition to daily emollients and in conjunction with moderately potent topical corticosteroid as rescue medication. Pimecrolimus twice daily was well tolerated by patients for up to 1 year with a few studies reporting an increased incidence of skin viral infections. More studies are needed to evaluate the efficacy of tacrolimus in preventing flares.

CONCLUSION: The twice weekly fluticasone propionate maintenance regimen can prevent recurrent relapse of AD and therefore reduces the need for acute intensive short courses of daily topical corticosteroid. Intermittent fluticasone propionate therapy is a viable option for long-term management of AD.

Table 1: Comparison of medication usage between two long-term treatment options

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Relapse is defined as the return of signs and symptoms after a period of remission while flare may be defined as an escalation of pre-existing signs and symptoms of disease. In atopic dermatitis, efficacy in relapse prevention has been demonstrated for topical fluticasone propionate in flare prevention for topical pimecrolimus. Depending on the threshold for defining a flare, it may be construed that all effective treatments for atopic dermatitis do so by flare prevention. In contrast, demonstrating in a randomized controlled trial, that relapse prevention is achievable with maintenance therapy during remission is a paradigm shift for clinicians who may previously have recommended treatment with onset of signs/symptoms of dermatitis, and discontinuation as these abate. It would be of particular interest to evaluate this concept of relapse prevention for topical calciuminhibitors as well. (Commentary by Dr. Tan)

<sup>1</sup> Hanifin J, Gupta AK, Rajagopalan R. Intermittent dosing of topical fluticasone propionate and in flare prevention has been demonstrated for topical fluticasone propionate. The present literature was analyzed to understand the current therapy options for long-term management of AD. The literature was examined following a search of MEDLINE and EMBASE databases. Search criteria included all articles on AD from January 1, 1995 to the present, published in English with human subjects including reviews, reports, and meta-analyses. Two different long-term maintenance therapy options were apparent during the review of the literature, one using topical corticosteroids and the other a combination of topical immunomodulators and topical corticosteroids. Discussion: Topical corticosteroids are widely prescribed for the treatment of AD and are considered to be the mainstay of AD therapy. They have been proven to be safe and efficacious in randomized, controlled trials for short-term (2 to 4 weeks) continuous use. The new TIMs, tacrolimus and pimecrolimus, have also been proven to be safe and efficacious in randomized, controlled trials for the short to medium term (6 months to 1 year) treatment of AD, and especially in the prevention of progression to flares. Randomized controlled clinical studies demonstrate that two long-term treatment options are viable for managing AD:

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ii) Pimecrolimus twice daily in addition to daily emollients and in conjunction with moderately potent topical corticosteroid as rescue medication. Pimecrolimus twice daily was well tolerated by patients for up to 1 year with a few studies reporting an increased incidence of skin viral infections. More studies are needed to evaluate the efficacy of tacrolimus in preventing flares.

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BACKGROUND: Fluticasone propionate is a novel and potent corticosteroid. It seems to have an improved therapeutic index on the basis of studies on skin thinning and suppression of hypothalamic-pituitary-adrenal axis. OBJECTIVE: We assessed the efficacy and safety of fluticasone propionate (FP) 0.05% cream once daily as compared with clobetasone butyrate (CB) 0.05% cream twice daily in children with atopic dermatitis (AD). METHODS: Twenty-two children (3 to 8 years old) with moderately active AD received either FP once daily or CB twice daily. Severity of AD was scored weekly by means of the modified Scoring of Atopic Dermatitis system (SCORAD) and treatment was either stopped when skin lesions were almost cleared (SCORAD < 9) or after 4 weeks. Cortisol excretion was determined by means of 24-hour urine before and after treatment. RESULTS: Twenty-one children completed the study. After 1 week of treatment, mean SCORAD significantly decreased in both treatment groups. After 2, 3, and 4 weeks cumulatively, 8, 12, and 16 children, respectively, were clinically healed (SCORAD < 9). No significant differences in efficacy were observed between the two treatments. Urinary cortisol excretion was not altered by either of the treatments. Two weeks after discontinuation of active treatment, mean SCORAD had increased to 22, but still was significantly lower than that at the beginning of the study.

CONCLUSION: Once-daily treatment with FP is as safe and effective as twice-daily treatment with CB in children with AD. All children experienced an exacerbation of AD within 2 weeks after treatment was withdrawn, indicating the need for long-term “intermittent” treatment.

Despite limited numbers of patients in this randomized double-blinded study, only 3 of 12 in the FP-treated group and 2 of 9 in the CB-treated group were not clinically “healed” at four weeks. Despite such limited numbers, the significance of these findings of equal efficacy in once daily FP and twice daily CB mirrors the efficacy of both in other reports in adults treated for atopic dermatitis. Given the differences in body surface area, and the difficulties encountered in urine collection in this study, other sources should be relied upon to confirm the safety of FP creme in children. Once daily therapy with FP creme, a potent steroid, is as effective as a moderately potent topical corticososteroid (CB creme) with the inherent better real-world compliance, and thus efficacy, and economy of once-daily application (Commentary by Dr. Kunynetz)

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Alefacept is the first biologic agent approved for the treatment of chronic plaque psoriasis in the United States. Alefacept, administered intravenously (i.v.) or intramuscularly (i.m.), was found to be well tolerated, safe, and efficacious in two pivotal phase 3 studies in patients with moderate to severe psoriasis. Treatment with i.v. alefacept was associated with a median duration of off-treatment response of 216 days (approximately 7 months). In a follow-up extension study to the phase 3 i.m. study, duration of therapeutic response was also examined. Patients who achieved a > or = 75% reduction in baseline Psoriasis Area and Severity Index (PASI 75) with the first course of alefacept 15 mg i.m. in the phase 3 study maintained a PASI 50 for a median duration of 209 days. In addition, the extension study demonstrated that a second course of i.m. alefacept is safe and well tolerated in patients with psoriasis.

In Canada, Alefacept is the only biologic agent to be approved to treat psoriasis. Since greater improvement is noted after a second 12 week course, a second course should be considered in patients with an initial suboptimal response. Results are similar for the intramuscular and intravenous formulations. In common with PUVA, Alefacept is a remittive agent. This contrasts with methotrexate, cyclosporine, retinoids and UVB phototherapy which require continuous treatment for disease control. (Commentary by Dr. Guenther)

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