

## Therapeutic Abstracts in Dermatology 2004-2005

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#### **Successful treatment of malignant melanoma in situ with topical 5% imiquimod cream**

Carolyn M, Michael K, Caron M, et al  
*Int. J. of Derma* 2005; 44: 428 – 434

Current treatment recommendations for malignant melanoma in situ include surgical excision with at least 0.5 cm margins. On the head or neck, obtaining adequate surgical margins for melanoma can be challenging and often disfiguring. In addition, some elderly patients may not be good surgical candidates and may request less aggressive interventions.

Imiquimod has been shown to induce immunologic activity by stimulating significant increase in numerous cytokines, including interferon- $\alpha$ , tumor necrosis factor (TNF) and interleukin - 12 (IL-). The use of adjuvant interferon therapy in the treatment of melanoma is well-established. We postulate that the topical agent, imiquimod, which is capable of inducing interferon production, may be an effective treatment of both LM and LMM, and in palliation of cutaneous metastases of invasive melanoma. Topical imiquimod can be used successfully for the treatment of malignant melanoma in situ on the face.

#### **Effective of topical corticosteroid application frequency on histamine – induced wheals**

Narasimha S, Srinivas C, Anil C. et al  
*Int. J. of Derma* 2005; 44: 425-427

Topical corticosteroids are the most commonly prescribed drugs for treating skin diseases. Appropriate guidelines for optimizing therapy with these agents are not fully established.

Very few studies have been conducted to assess the effect of corticosteroid application frequency to attain maximum benefit with minimum side-effects.

A study was done to compare the efficacy of twice-daily and alternate-day applications of clobetasol propionate (0.05%) and compare whether an initial once-daily application followed by a subsequent alternate-day application is as effective as a once-daily application. Conclusion a once-daily application of clobetasol propionate (0.05%) is likely to provide the required therapeutic effect.

#### **Anticonvulsant hypersensitivity syndrome**

Kaminsky A, Morenom M, Diaz M, et al  
*Int. J. of Derma* 2005; 44: 594-598

Anticonvulsant hypersensitivity syndrome was first described by Chaiken et al. in 1950. it is an unpredictable and potentially severe reaction with an incidence ranging between 1 in 1000 and 1 in

10,000 exposures. Its importance has now been fully acknowledged, as it represents the major cause of hospitalization for dermatologic complications in patients under treatment with anticonvulsant drugs. Patients infected with the human immunodeficiency virus (HIV) and cancer carriers are at a higher risk for this adverse drug reaction.

Anticonvulsant hypersensitivity syndrome (AHS) characterized by the appearance of fever, skin rash and internal organ involvement.

Phenytoin, Phenobarbital and carbamazepine are the most frequent aromatic anticonvulsants causing the reaction. This syndrome occurs 1-8 weeks after the initial drug exposure but, even though glucocorticoids appear to be useful in severe cases, discontinuation of the drug has been found to be essential in the resolution of symptoms.

Reexposure to anticonvulsant drugs is followed by a quick, severe reappearance of all symptoms, which strongly argues against their prescription. The incidence of cross-reactivity among the aromatic anticonvulsants is greater than 75%.

First-degree relatives of an afflicted individual have a fourfold higher risk of drug sensitivity than the population at large. Therefore, family counseling is of the utmost importance in the attempt to ensure efficient management of these patients.

#### **4% Hydroquinone versus 4% hydroquinone, 0.05% dexamethasone and 0.05% tretinoin in the treatment of melasma: a comparative study**

Astaneh R, Farboud E, Nazemi M,  
*Int. J. of Derma* 2005; 44, 599-601

Melasma is an acquired irregular brown or sometimes graybrown hyperpigmentation of the face and occasionally the neck, usually occurring in women, and more prevalent in persons of Hispanic origin living in sunny locations. Although melasma is primarily associated with pregnancy and ocp consumption, other influences such as genetic, racial, endocrine and cosmetic factors seem to be involved. It is generally accepted that sunlight and genetic factors play major roles in the pathogenesis of this condition.

A randomized, controlled, double-blind clinical study was conducted on 64 patients with melasma, in order to compare 4% hydroquinone cream with a combination product, containing 4% hydroquinone, 0.05% tretinoin and 0.05% dexamethasone, that can be applied as a single cream.

This clinical trial demonstrates that addition of tretinoin and dexamethasone to a cream containing hydroquinone further improves the usefulness of hydroquinone in reducing melasma.

This combination product is indicated for the short-term treatment of moderate to severe melasma of the face with use of sun screen. Compounded preparations are often effective in patients that have failed to respond to lower concentrations of hydroquinone. With controlled use and monitoring, side-effects from these preparations have proved to be minimal.



### **Etanercept and psoriasis, from clinical studies to real life**

Jacob, S., Sergay A, Francisco A, et al.  
*Int. J. of Derm* 2005; 44 688 – 691

Etanercept was the first Food and Drug Administration (FDA)-approved treatment for psoriatic arthritis. This dimeric fusion protein inhibits the pro-inflammatory cytokine, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), from interacting with cell surface receptors, and renders it biologically inactive. Clinically, the effect in psoriatic arthritis and psoriasis is profound. On the flip-side, adverse side-effects are minimal, with the most commonly reported being mild injection site reactions, as seen in rheumatoid arthritis.

This study is to determine whether etanercept therapy enables long-term psoriasis patients to discontinue systemic psoriatic therapy.

They concluded that Etanercept is a safe and effective therapy in chronic moderate to severe psoriasis. For patients who are receiving systemic therapy for their disease and alternative therapy is warranted. Etanercept can be added with the aim to discontinue the other systemic agents.

### **Treatment of keloids and hypertrophic scars with dermojet injections of bleomycin: a preliminary study**

Saray, Y., Gulec T  
*Int. J. of Derm* 2005; 44 777-784

Keloids and hypertrophic scars (HS) are abnormal healing responses characterized by excessive accumulation of extracellular matrix and by over-abundant collagen formation in particular. These lesions occur after a variety of cutaneous injuries, including surgery, burns, dermal trauma, acne, and some even arise spontaneously. Keloids and HS can cause physical disfigurement, restricted range of motion, bothersome symptoms, and psychological problems, and yet there is no consensus in the literature regarding appropriate therapy. Several treatment modalities, such as intralesional (IL) injections of corticosteroids or 5-fluorouracil, surgical excision, cryotherapy, radiotherapy, have been used with variable success.

This study was to determine the efficacy and safety of intralesional jet injection of bleomycin as therapy for keloids and hypertrophic scars that are unresponsive to intralesional steroid injection.

They concluded that intralesional jet injection of bleomycin is an effective and safe method of treating keloids and hypertrophic scars that are unresponsive to intralesional steroid therapy.

### **Isotretinoin Therapy and Mood Changes in Adolescents with Moderate to Severe Acne**

Chia, C., Lane, W., Chibnall J, et al.  
*ARCH Dermatol* 2005; 141 557 – 560

Acne can be a painful and disfiguring disease that leaves some

individuals with permanent physical and psychological scars. Isotretinoin (13-cis-retinoic acid, first marketed as Accutane; Hoffmann-LaRoche Inc, Nutley, NJ), is a synthetic vitamin A analogue approved by the Food and Drug Administration in 1982 for the treatment of severe cystic acne is the most effective treatment available for acne that is unresponsive to other therapies. An increasing number of cases of depression and suicide in patients using isotretinoin reported to the Food and Drug Administration has prompted much concern and yielded new labeling and patient-informed consent regarding possible psychiatric side effects.

The study of 101 patient uses isotretinoin in the treatment of moderate-severe acne in adolescents did not increase symptoms of depression. On the contrary, treatment of acne either with conservative therapy or with isotretinoin was associated with a decrease in depressive symptoms.

### **0.1% Tacrolimus Ointment for the Treatment of Intertrigo**

Chapman, M., Brown J., Linowski, G.  
*ARCH Dermatol* 2005; 141 787

Intertrigo is a combination of infectious, mechanical, and inflammatory changes of the skin folds that can be recurrent and chronic. Friction between skin folds and increased moisture promote an irritated cutaneous environment that increases the chance of infection. The combination of these factors leads to an inflammatory process.

In this small study, 0.1% tacrolimus ointment proved to be rapidly effective, as most patients were clear or 75% clear after one week of application. Only twice a day one of nine patients failed to clear after six weeks of treatment. Burning at the application site was the most common adverse effect, but it was usually transient and tolerable.

### **Safety and Efficacy of 5% Imiquimod Cream for the Treatment of Skin Dysplasia in High-Risk Renal Transplant Recipients**

Victorica, B., Atkins, C., Ghali, L., et al.  
*ARCH Dermatol* 2005; 141: 985 - 993

Immunosuppressed renal transplant recipients (RTRs) experience significant morbidity from cutaneous viral warts (VWs), actinic keratoses (AK), Bowen disease (carcinoma in situ [CIS]), cutaneous squamous cell carcinoma (SCC), and basal cell carcinoma (BCC). Owing to the lifelong requirement for immunosuppression in RTRs, these skin abnormalities tend to be difficult to treat, with their multiplicity of lesions, frequent recurrences, and resistance to many treatment modalities.

A study was done to evaluate the safety and efficacy of 5% imiquimod cream for cutaneous dysplasia in high-risk renal transplant recipients.

They concluded that topical 5% imiquimod cream seems to be safe on skin areas up to 60 cm<sup>2</sup> in renal transplant recipients. It may be effective in reducing cutaneous dysplasia and the frequency of squamous tumors developing in high-risk patients.



### **Treatment of Early-stage Mycosis Fungoides with Twice a week Applications of Mechlorethamine and Topical Corticosteroids**

Quatrebarbes, J., Esteve, E., Bagot M., et al.  
ARCH Dermatol 2005; 141: 1117 – 1120

Mycosis Fungoides (MF) is the most common type of cutaneous T-cell lymphoma. Its incidence is increasing in the United States and Europe. It is histologically characterized by an infiltrate of epidermotropic atypical T. lymphocytes. It has been demonstrated that patients with early-stage MF (T1) have a long-term survival outcome that does not differ significantly from an age, sex, and race matched population. A study was done to determine if a therapeutic regimen of twice a week application of Mechlorethamine hydro-chloride and betamethasone dipropionate cream is effective in the treatment of early-stage mycosis Fungoides while increasing cutaneous tolerance. They found that a regimen of twice-weekly applications of Mechlorethamine and betamethasone cream is an effective treatment for early stage mycosis Fungoides. The decreased frequency of applications provides an advantage to the patient by being easy to use with limited adverse effects.

### **Antibiotic Treatment of Acne May Be Associated With Upper Respiratory Tract Infections**

Margolis, D., Bowe, W., Hoffstad, O., et. al.  
ARCH Dermatol 2005; 141: 1132 - 1136

Concerns have been expressed regarding the overuse of antibiotics, which has been associated with the emergence of resistant organisms, increase in the frequency of human exposure to pathogenic organisms, and an increase in infectious illnesses. Surprisingly, very few studies have been conducted on populations of patients who have actually been exposed to antibiotics for long periods.

This study done to determine if the long-term use of antibiotics for the treatment of acne results in an increase in either of two common infectious illnesses: upper respiratory tract infections (URTIs) or urinary tract infections.

They conclude that patients with acne who were receiving antibiotic treatment for acne were more likely to develop a URTI than those with acne who were not receiving such treatment. The true clinical importance of our findings will require further investigation.

### **Rosaceiform Dermatitis as Complication of Treatment of Facial Seborrheic Dermatitis With 1% pimecrolimus Cream**

Gorman, C., White, S.  
ARCH Dermatol 2005; 141: 1168

Two case reports with the observation of rosaceiform dermatitis after treatment of facial seborrheic dermatitis with 1% pimecrolimus cream supports the finding that this complication is not isolated to treatment of atopic dermatitis and is related to this class of medication. The

incidence of this complication remains unknown, and further study will be required to determine which patients are at risk.

### **0.1% Tacrolimus Ointment in the Treatment of Discoid Lupus Erythematosus**

Hefferman, M., Nelson, M., Smith, D., et. al.  
ARCH Dermatol 2005; 141 1170-1171

Discoid lupus erythematosus (DLE), which is an autoimmune inflammatory disorder of the skin, often leads to scarring and alopecia. Current treatment options include topical and systemic glucocorticoids, antimalarial agents, and thalidomide. These treatments are often limited by a lack of efficacy or by adverse effects.

We conducted an open-label pilot study using 0.1% tacrolimus (Protopic) ointment for the treatment of five subjects with biopsy-proven DLE.

We found the relatively early and sustained improvement in the subjects with DLE who were treated with tacrolimus is promising. Large controlled trials are warranted.

### **Efficacy and tolerability of three different doses of oral pimecrolimus in the treatment of moderate to severe atopic dermatitis: a randomized controlled trial**

Wolffk, Fleming C., Hanifin, J., et. al.  
British J. of Dermatology 2005; 152: 1296-1303

Background adult atopic dermatitis (AD) can seriously affect quality of life of patients and their families, and patients' disease is frequently not satisfactorily controlled with topical therapy. There is a need for alternatives to topical treatment in patients with moderate to severe AD. We investigated the efficacy and safety of oral pimecrolimus, and to determine the response to three different doses in the treatment of AD.

We demonstrated the clinically relevant efficacy and short-term safety of oral pimecrolimus in adults with moderate to severe AD. Longer-term studies in larger cohorts are now required.

### **Therapy of noninfectious granulomatous skin diseases with fumaric acid esters.**

Breue K, Gutzmer, Volker B., et. al.  
British Journal of Dermatology 2005; 152: 1290-1295

Noninfectious granulomatous skin diseases are inflammatory disorder of unknown aetiology which are often recalcitrant to common anti-inflammatory treatment regimens. Recently, in several case reports, fumaric acid esters (FAE) have proven to be beneficial in granulomatous skin disease. We investigate the therapeutic efficacy of FAE for the treatment of granulomatous skin diseases.

Our data indicate that FAE may be considered for the treatment of recalcitrant granulomatous skin disease.

**Efficacy and safety of methotrexate in recalcitrant Cutaneous lupus erythematosus: results of a retrospective study in 43 patients**

Wenzel J., Brahler S., Bauer R., et. al.

British Journal of Derma 2005; 153(1): 157 - 162

The therapy of cutaneous lupus erythematosus (CLE) is often challenging, especially in patients resistant to topical treatment and established first-line systemic drugs such as antimalarials. Systemic corticosteroids are effective, but their use is limited due to well-known side-effects, especially in long-term treatment.

Our study supports earlier findings reporting the efficacy of low-dose MTX in CLE lesions, particularly in recalcitrant clinical courses. MTX treatment appears to be safe if patients are carefully selected and monitored, with particular attention to side-effects and contraindications.

**Thalidomide: dermatological indications, mechanisms of action and side-effects**

Wu J., Huang D., Pang K., et. al.

British Journal of Derma 2005; 153(2): 254 – 273

Thalidomide was first introduced in the 1950s as sedative but was quickly removed from the market after it was linked to cases of severe birth defects. However, it has since made a remarkable comeback for the U.S. Food and Drug Administration approved as use in the treatment of erythema nodosum leprosum. Further, it has shown its

effectiveness in unresponsive dermatological conditions such as actinic prurigo, adult Langerhans cell histiocytosis, aphthous stomatitis, Behcet's syndrome, graft-versus-host disease, Cutaneous sarcoidosis, erythema multiforme, Jessner-Danof lymphocytic infiltration of the skin, Kaposi sarcoma, lichen planus, lupus erythematosus, melanoma, prurigo nodularis, pyoderma gangrenosum and uraemic pruritus.

**Topical pimecrolimus in the treatment of genital lichen planus: a prospective case series**

Lonsdale Eccles A., Velangi, S.

British Journal of Derma 2005; 153(2): 390 – 394

A potent topical steroid is the conventional therapy for genital lichen planus (GLP). Side-effects or steroid resistance can be encountered and second-line therapy such as topical tacrolimus may be required. Tacrolimus may be poorly tolerated in genital skin because of a burning sensation. In addition, there is impairment of langerhans cell function, raising concerns about its long-term use. These adverse effects may not be as marked with pimecrolimus.

We have found that topical pimecrolimus 1% cream is an effective treatment for GLP. Local irritation can limit its use, but it may be better tolerated than topical tacrolimus: three of our complete responders had previously been intolerant of tacrolimus. Topical pimecrolimus may be a valuable second-line treatment for patients with steroid-related side-effects or steroid-resistant GLP