PA-01: A meta-analysis to evaluate the efficacy and safety of adapalene-benzoyl peroxide topical gel in black subjects with mild or moderate acne

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BACKGROUND: Adapalene, a synthetic retinoid analogue, and benzoyl peroxide (BPO), an effective antimicrobial agent, are currently available at concentrations of 0.1% and 2.5%, respectively, as a fixed combination gel for the treatment of acne. OBJECTIVE: This meta-analysis was conducted to investigate the safety and efficacy of adapalene-benzoyl peroxide (A-BPO) in self-identified black subjects based on the data from 3 trials. METHODS: Results from 3 multicenter, randomized, double-blind, vehicle-controlled, clinical trials of A-BPO gel were analyzed in a prospective subgroup meta-analysis. Subjects were assessed at weeks 1, 2, 4, 8, and 12 for efficacy and safety. RESULTS: The analysis included 238 self-identified black subjects in the A-BPO and vehicle treatment groups who were treated for 12 weeks. This subgroup was comprised primarily of women with Fitzpatrick skin types V and VI and a mean age of 21.3 years. After 12 weeks of treatment, significantly more subjects achieved investigator global assessment (IGA) success with A-BPO (n = 121; 31.4%) than with vehicle (n=117; 14.5%) (P<.001). Significant reductions in median total lesions were observed with A-BPO compared to vehicle at all postbaseline visits (P<.01). Most subjects did not experience cutaneous irritation. Of those who did, their worst tolerability scores were mostly none or mild for all treatment groups. Most reported adverse events (AEs) were mild in severity. Two subjects reported serious AEs that were unlikely related to the study treatment: 1 AE of worsening depression in the A-BPO group and 1 AE of miscarriage in the vehicle group. Four subjects discontinued treatment due to AEs. CONCLUSION: Treatment with A-BPO in black subjects with mild to moderate acne was effective and well tolerated. CORRESPONDING AUTHOR: Warren Winkelman, MD (standing in for Nabil Kerrouche in France); Galderma Laboratories, LP; 14501 North Freeway, Fort Worth, TX 76177. E-mail: warren.winkelman@galderma.com CONFLICTS: A Alexis has served as a consultant and advisory board member for Galderma. W Winkelman is an employee of Galderma Laboratories, LP. ACKNOWLEDGEMENTS: Study funded and poster/editorial support provided by Galderma Laboratories, LP.

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PA-02: A randomized placebo-controlled trial of bimatoprost for androgenic alopecia in men

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BACKGROUND: Androgenic alopecia (AGA) in men is marked by thinning hair or male pattern balding typically starting at the vertex area of the scalp. Bimatoprost (BIM), a synthetic prostamide approved for treatment of hypotrichosis of the eyelashes, is being investigated for treatment of AGA. OBJECTIVE: To evaluate the efficacy and safety of once-daily topical BIM solution for increasing scalp hair growth in men with AGA. METHODS: In a phase 2 multicenter trial, men 18-49 years of age with mild to moderate AGA were randomized in a 1:1:1:1 ratio to receive in a double-blind manner BIM 0.3%, 0.1%, 0.03%, or vehicle applied once daily, or open-label minoxidil 5% (MIN) applied twice daily to the vertex area of the scalp for 6 months; subjects were followed for 2 months after the last dose of study medication. The primary efficacy measure was change from baseline in target area hair count (TAHC, terminal hairs/cm2 by digital image analysis) and subject self-assessment (SSA) of change in scalp hair growth vs baseline. Key secondary efficacy measures included target area hair width (TAHW, mm/cm2 by digital image analysis) and a blinded photographic assessment of change in scalp hair growth vs baseline by global panel review (GPR) on a 7-point scale (-3 to +3) by an independent panel of 3 dermatologists. Safety measures included adverse events, local tolerability assessments, clinical laboratory parameters, physical examinations, vital signs, and electrocardiograms (ECGs). RESULTS: A total of 307 men with AGA were included in efficacy and safety analyses (61 subjects each in the BIM 0.3%, BIM 0.1%, and MIN groups and 62 subjects each in the BIM 0.03% and vehicle groups). For the double-blind arms at month 6, mean percent change from baseline TAHC was significantly greater with BIM 0.3% (11.1%, P=.008) vs vehicle (3.3%) (BIM 0.1%: 5.3%; BIM 0.03%: 4.2%). At month 6, the distribution of SSA scores in the BIM 0.3%, 0.1%, and 0.03% groups was not significantly different vs vehicle. Mean percent change from baseline at month 6 in TAHW was significantly greater with BIM 0.3% (10.4%, P=0.005) vs vehicle (1.7%) (BIM 0.1%: 4.3%; BIM 0.03%: 2.9%). GPR assessments (percentage of photographs
PA-03: A simple, reliable, and effective store-and-forward teledermatology system

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BACKGROUND: Store-and-forward teledermatology is an emerging technology with the potential to initiate a paradigm shift in how patients and healthcare providers (HCPs) interact. Information communication technologies, such as tablets, may provide an easily accessible interface to facilitate information exchange between patients and HCPs. OBJECTIVE: A pilot study was conducted to investigate the use of a tablet based numeric rating scale to track improvement of a plaque psoriasis target lesion treated with clobetasol propionate 0.05% spray. METHODS: This was a prospective open-label, single-arm, single-site study; Subjects with plaque psoriasis were enrolled for study; Target lesion of at least 1cm x 1cm was treated with clobetasol propionate 0.05% spray (CPS) for 15 days. Assessments: The assessment scales and tablet application were developed using open-source software (Google Apps). Assessments were made by the investigator and the subject and entered directly into the tablet. Photographs of target lesion were taken using tablet camera. Adverse events were directly recorded into the tablet. RESULTS: The results indicate that such a system is simple, cost-effective, reliable, and suitable to use in clinical studies as well as in a clinical setting. Improvements for all assessments were similar between investigators and subjects indicating each viewed target-lesion improvements similarly. This suggests that subjects will give reliable and accurate information regarding their disease state when using a tablet-based rating system. LIMITATIONS: This was a small pilot study that was not powered. A larger, powered study would confirm the results and the utility of this methodology. CONCLUSION: This tablet-based rating system is a simple, reliable, and effective teledermatology medium suitable to measure and track disease progression and treatment effects in studies as well as in a clinical setting. CORRESPONDING AUTHOR: Warren Winkelman, MD; Galderma Laboratories, L.P.; 14501 North Freeway, Fort Worth, TX 76177. E-mail: warren.winkelman@galderma.com CONFLICTS: W Winkelman is an employee of Galderma Laboratories, L.P.

PA-04: Adapalene gel, 0.3% is efficacious in reducing acne lesions in adult women

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BACKGROUND: Recent reports suggest an increasing prevalence in adults. In particular, there is an increasing prevalence in adult women, affecting an estimated 40%-50% of women over the age of 20, a difficult population to treat. OBJECTIVE: Investigate the effect of adapalene gel 0.3% in adult women. METHODS: Retrospective analysis, subgroup analysis of data pooled from 2 pivotal studies; Adult women 18 or older; 12 weeks of adapalene gel, 0.3%, adapalene gel 0.1%, or vehicle applied once daily at night; Efficacy, safety, and tolerability of adapalene gel, 0.3% compared to vehicle in subjects with acne vulgaris; Inflammatory, noninflammatory, and total lesion counts were assessed at baseline and week 12. RESULTS: The results showed a statistically significant difference favoring adapalene gel, 0.3% for the mean percent reduction in total lesion count at Week 12 (P = .045). LIMITATIONS: This was a post hoc analysis of a subgroup population. A prospective study that enrolled just this population would confirm the results. CONCLUSION: Subgroup analysis shows that adapalene gel, 0.3% is efficacious in reducing acne lesions in adult females with acne vulgaris; In the phase 3 study, tolerability for adapalene gel, 0.3% was equivalent to adapalene gel, 0.1%. CORRESPONDING AUTHOR: Diane Berson, MD; Weill Medical College of Cornell University; New York Presbyterian Hospital; 211 E 53rd St # 3, New York, NY 10022. E-mail: dsberson@aol.com CONFLICTS: D Berson is an investigator of Galderma Laboratories, L.P. A Alexis has served as a consultant and advisory board member for Galderma.
PA-05: Calcipotriene counteracts betamethasone-induced decrease in biomarkers related to skin atrophy

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BACKGROUND: The calcipotriene/betamethasone dipropionate two-compound suspension is widely used for topical treatment of psoriasis vulgaris. It has been hypothesized that the addition of calcipotriene to the steroid component may counteract steroid-induced skin atrophy. Decreases in collagen synthesis and degradation (suppression of MMPs), hyaluronic acid (HA) and epidermal thickness have all been associated with skin atrophy. OBJECTIVE: To compare the skin atrophogenic potential of the calcipotriene/betamethasone dipropionate combination with the respective monotherapies by investigating their effect on these biomarkers in vitro in fibroblast and keratinocyte cultures, ex vivo in a new skin explant model (NativeSkinTM) and in vivo in minipigs.

METHODS: For ex vivo and in vivo studies, calcipotriolene 0.005% and betamethasone dipropionate 0.064%, the corresponding vehicle suspension and the mono-components formulated in the vehicle suspension were applied. Monolayer cultures were treated with 100 nM calcipotriene, 1 mcM betamethasone, 100 nM calcipotriene/1 mcM betamethasone (ratio 1:10 as in the fixed-combination product) or a corresponding vehicle control (0.1% dimethyl sulfoxide). Göttingen minipigs were dosed topically once daily with the suspension for a total of four weeks. RESULTS: Betamethasone dipropionate mono-treatment induced a slight but consistent reduction in collagen I synthesis by fibroblasts in vitro and ex vivo. Secretion of MMP1 and MMP3 from both fibroblasts and keratinocytes was also inhibited by betamethasone dipropionate mono-treatment. In contrast to betamethasone, calcipotriene and the combination increased collagen I synthesis both in vitro and ex vivo. Similarly, an opposing effect of calcipotriene and betamethasone was also seen on MMP expression. Betamethasone dipropionate reduced the secretion of HA in both fibroblast and keratinocyte cultures. Calcipotriene did not affect the secretion of HA in fibroblast cultures while the combination reduced secreted levels of HA to that obtained by betamethasone mono-treatment. However, in keratinocyte cultures calcipotriene enhanced the secretion of HA and no significant change was seen with the combination treatment. In vivo, treatment with betamethasone dipropionate suspension significantly decreased epidermal thickness in minipigs compared with the vehicle group. By contrast, treatment with calcipotriene suspension or the combination did not reduce epidermal thickness in minipigs. CONCLUSION: In conclusion, these data indicate that the calcipotriene component of the two-compound suspension counteracts the betamethasone dipropionate-induced decrease in biomarkers related to skin atrophy. CORRESPONDING AUTHOR: H. Norsgaard, LEO Pharma A/S; Industrieparken 55; DK-2750 Ballerup; Denmark. CONFLICTS: H Norsgaard has nothing to disclose.

PA-06: Clinical pearls with ingenol mebutate treatment in elderly patients with actinic keratosis in a community dermatology practice

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BACKGROUND: The management of patients with actinic keratosis (AK) includes both lesion-directed and field-directed therapies to target discreet, isolated lesions as well as skin with confluent visible and subclinical AKs. OBJECTIVE: To retrospectively analyze the charts of patients from a community dermatology practice and describe their results with ingenol mebutate treatment of AK. METHODS: The chart review extracted information on the patients’ medical history and demographics, pertinent history of AK and skin cancer, and treatments for those conditions. Analysis of the patients’ current treatment course with ingenol mebutate included data on the size and location of treatment areas, local skin reactions, adverse events, short-term efficacy, and long-term follow-up. RESULTS: Ingenol mebutate was used to treat AK in 135 patients from January 2012 to January 2013. Of these, 16 patients treated a second body site, and 3 patients treated a third site, for a total of 154 treatments. These patients had a prolonged history of AK that included prior treatment with cryosurgery and/or topical agents. Many of these patients also had a history of nonmelanoma skin cancer. In the current course of treatment with ingenol mebutate, 78% of patients presented with sun-damaged skin with >15 AKs, including AKs that were recurrent or hyperkeratotic. The majority of patients, 77%, received cryosurgery to all visible lesions 2 weeks before their first ingenol treatment course. Ingenol mebutate gel, 0.015%, was used to treat the face in 77 patients, the scalp in 45 patients, and the chest in 1 patient; ingenol mebutate gel, 0.05%, was used to treat the forearms and/or hands in 31 patients. Treatment areas were typically >25 cm² in size and included portions of the face, the entire scalp, or entire forearms. Local skin reactions consisting of mild to moderate erythema and flaking/scaling generally resolved within 1 week and were not treated in most patients. Complete and partial clearance was defined as 100% and ≥75% clearance, respectively, of baseline and emergent AKs. At 1 to 4 months after treatment of the face, the rates of complete and partial clearance were 44% and 55%, respectively. The rate of complete clearance for patients who treated areas of the face >100 cm² in size was less than that for patients who treated areas ≤100 cm² in size. At 1 to 4 months after treatment of the scalp, the rates of complete and partial clearance for the scalp were 22% and 67%, respectively; for forearm and hand AK, >80% of patients demonstrated ≥75% improvement. At evaluations up to 1 year after ingenol mebutate treatment, emergent lesions were recognized in the treated field and treated with cryosurgery. Patients reported high treatment satisfaction and indicated that they would use ingenol mebutate on other body sites with AK. CONCLUSION: Dermatology patients treated in
a community-based practice achieved substantial clearance of AK on head and body sites following treatment with ingenol mebutate gel. The proportion of patients who achieved 100% clearance on the face was higher for treatment areas ≤100 cm² than for treatment areas >100 cm². Ingenol mebutate is an effective, well-tolerated topical treatment for managing the burden of AK in sun-damaged skin.

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PA-07: Cutaneous manifestations in hypereosinophilic syndromes
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BACKGROUND: Hypereosinophilic syndromes (HES) are characterized by persistent eosinophilia >1500/mm³ with end organ manifestations, the most common of which are dermatologic. The range of cutaneous findings has not been systematically examined in a large cohort of well-characterized HES subjects to date. OBJECTIVE: In this study, we sought to identify and characterize the skin findings associated with HES. METHODS: Charts of 317 subjects with eosinophilia >1500/mm³ evaluated at the National Institutes of Health (NIH) from 1983 to 2013 on a clinical protocol to study eosinophilic disorders were reviewed. Epidemiologic, molecular, clinical, laboratory and histological records were examined, and all subjects with reported skin involvement identified. Skin biopsy records were reviewed and correlated with physical exam findings. RESULTS: Approximately 59% (188/317) of subjects had documented cutaneous findings. Of these, 35.64% (67/188) had idiopathic HES, 13.83% (26/188) had lymphocytic variant HES, 10.64% (20/188) had myeloproliferative HES, and 39.89% (113/188) had other causes of marked eosinophilia. The mean age of initial presentation in this study was 44.05 ±19.45 (SD) years (range 3 months – 85 years), with equal male to female prevalence. Although the most common dermatological findings were pruritus (51.26%), urticaria (13.84%), atopic dermatitis (11.64%) and angioedema (10.69%), unusual manifestations, such as skin ulcers and bullous lesions, were seen in some subjects. Skin biopsies were done in 39% (73/188) of cases. The most common clinical diagnoses after pathologic examination were atopic dermatitis (22.47%), urticaria (12.36%), eosinophilic cellulitis (6.74%) and eosinophilic fasciitis (6.74%). LIMITATIONS: This study has several limitations. Due to the retrospective nature of the analysis, complete data sets were not available for all subjects. Furthermore, the fact that biopsies were not performed systematically in all subjects may have resulted in bias towards particular histopathological diagnoses. Finally, medication administration at the time of presentation may have confounded the ability to make a histologic diagnosis in some cases. CONCLUSION: HES is a heterogeneous multisystem disease, which often presents with cutaneous manifestations. Although the majority of dermatologic manifestations identified were not specific for eosinophilic disease, a high percentage of subjects who underwent skin biopsy had evidence of eosinophilic infiltration. CORRESPONDING AUTHOR: Annalise O. Abiodun; National Institutes of Health, National Institute of Allergy and Infectious Diseases; NIH/NIAID/Eosinophil Pathology Unit; 4 Memorial Drive, Bldg 4, Room B1-28; Bethesda, MD 20892. E-mail: Annalise.Abiodun@nih.gov

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PA-08: Cutaneous tolerability and subject satisfaction of an over-the-counter cleansing and moisturizing regimen in subjects aged 7 to 11 years with acne prone skin
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BACKGROUND: To investigate a commercially available foaming facial wash and moisturizer SPF 30 skin care regimen specifically formulated for acne-prone skin in subjects 12 years of age and older. OBJECTIVE: To show a commercially available foaming facial wash and moisturizer SPF 30 skin care regimen specifically formulated for acne-prone skin can be safe and tolerable in subjects 12 years of age and older. METHODS: Open-label, single-center study; Boys and girls, 7 to 11 years of age, with acne-prone skin; Global severity of acne (GSA) score of 1 (almost clear) or 2 (mild) and any oiliness evaluation score ≥ 1 (mild). A foaming facial wash was applied twice daily and a facial moisturizer SPF 30 was applied once daily for duration of 22 days. RESULTS: Overall, there was a favorable response to all subject satisfaction questions asked at study end. Most subjects responded that they liked using the foam wash and moisturizer and would keep using both of these products. LIMITATIONS: A larger study population that included teenagers would confirm and strengthen the results of the study. CONCLUSION: The foam wash and moisturizer were safe and well-tolerated in subjects 7 to 11 years of age. Most subjects responded favorably to all subject satisfaction questions for both products. CORRESPONDING AUTHOR: Staci Brandt; Galderma Laboratories, L.P.; 14501 North Freeway, Fort Worth, TX 76177. E-mail: staci.brandt@galderma.com

CONFLICTS: S Brandt is an employee of Galderma Laboratories, L.P.
PA-09: Dysregulation of Heat Shock Proteins in Skin Basal Cell Carcinoma

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BACKGROUND: Pathogenesis of basal cell carcinoma (BCC), the most common malignancy in Caucasian population is complex and strongly connected with environmental and genetic factors. Heat shock proteins (HSPs) belong to a highly conserved in-evolution group of proteins involved in stress response and protein folding. HSPs also exert other regulatory functions important for cell survival or differentiation. However, there is a shortage of information on HSPs role in development and propagation of BCC. OBJECTIVE: To evaluate the presence, relative expression and localization of HSP27, HSP60, HSP90 and HSP105 in BCC and normal skin. METHODS: A total of 12 BCC skin biopsies and 12 healthy skin specimens (the control group) were served as material for the study. All specimens were stained using immunofluorescence techniques with monoclonal antibodies directed against the chosen proteins. RESULTS: In normal skin, HSP105 had distinguished localization in the cytoplasm of keratinocytes of squamous and granular layers of epidermis, but not in the stratum basale. A similar pattern was observed in superficial BCC, however, the stain showed a degree of heterogeneity (eg, keratinocytes with very high and very low levels of HSP105 were seen) while BCC cells were negative. In nodular BCC, expression of HSP105 decreased significantly in the epidermis and was undetectable in large nodular BCCs. Furthermore, HSP105 expression was very weak to absent in neoplastic tissue of both superficial and nodular BCC. HSP27 immunoreactivity was present in differentiated keratinocytes of the stratum granulosum and in corneocytes of normal skin. However, selected cells of stratum basale also showed HSP27 immunoreactivity. In the skin involved either by superficial or nodular BCC the HSP27 immunoreactivity was slightly increased in the non-neoplastic epidermis and was very weak in tumor cells. However, degree of heterogeneity was noted with some central areas of the tumor being positive, to others showing only few positive cells for HSP27. Concerning HSP60, it showed pronounced expression in the stratum basale as well as intense expression in other layers including selected cells of the stratum corneum. Moreover, HSP60 immunoreactivity was present in the mitochondria of epidermal cells. Interestingly, significantly higher immunoreactivity of HSP60 was detected in the basal layer of keratinocytes forming BCC nodules as well as in keratinocytes in stratum basale. The intensity of staining decreased towards the center of the lesion. These changes in HSP60 might reflect activity of mitochondria in neoplastic and normal keratinocytes. HSP90 expression was relatively weak and mainly in nuclei of keratinocytes in the epidermis. Even weaker HSP90 immunoreactivity was detected in superficial BCC. However, in some biopsies of nodular BCC, selected cells or patches of cells within the tumor were shown to have high levels of HSP90. Double staining of BCC sections with HSP27 and HSP60 antibodies have shown that distinct regions of higher immunoreactivity for those proteins could reflect metabolic and functional changes in cells during the growth of neoplastic tissues. Similarly, high level of HSP90 expression was shown in a selected population of dermal cells, while not well pronounced in the epidermis and skin lesions. CONCLUSION: HSPs are essential factors regulating and supporting cell development not only under physiological, but also under pathological conditions. Taking into consideration unique functions of each of the HSPs, the observed changes in the pattern of expression and localization in BCC lesions may shed new light on the development of this disease. CORRESPONDING AUTHOR: Michal Sobjanek; Department of Dermatology, Venerology and Allergology, Medical University of Gda´nsk, Debinki 7 str, 80-952 Gdans, Poland. E-mail: sobjanek@wp.pl

CONFLICTS: The authors have no relationships to declare.

PA-10: Effectiveness of adapalene/ benzoyl peroxide gel in the first four weeks of treatment in acne patients

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BACKGROUND: To help physicians and patients establish a realistic treatment expectation for the first 4 weeks of therapy, OBJECTIVE: A pooled analysis was conducted to specifically evaluate the effectiveness and tolerability achieved in the first 4 weeks of therapy. METHODS: Data from 14 studies, including 4 large vehicle-controlled studies (one with patients as young as 9 years of age), were pooled to evaluate the effectiveness and tolerability of adapalene/benzoyl peroxide gel (A-BPO) 0.1%/2.5% among acne subjects during the first 4 weeks of treatment. A total of 2,358 subjects between 9 years and 61 years old were treated with A-BPO gel 0.1%/2.5%. In most of these studies, A-BPO gel 0.1%/2.5% was used for 12 weeks. Inflammatory lesion counts, noninflammatory lesion counts, total lesion counts, and investigator global assessment scores were the endpoints. RESULTS: Inflammatory, noninflammatory, and total lesion counts decreased with A-BPO gel 0.1%/2.5% use, showing a 40%-50% reduction from baseline after the first 4 weeks of use. A-BPO gel 0.1%/2.5% was well tolerated among different skin types, ages, and genders, with most of the worst tolerability assessments being none or mild. LIMITATIONS: This was a post hoc analysis using data from different studies. CONCLUSION: A-BPO gel 0.1%/2.5% was well tolerated and reduced approximately half of the inflammatory and noninflammatory lesion counts at 4 weeks. The effects seen in the first 4 weeks from these studies are consistent with those already demonstrated in individual vehicle-controlled studies. These observations provide a framework of expectations for A-BPO gel 0.1%/2.5% treatment during the first 4 weeks of treatment for clinicians to discuss with their patients. CORRESPONDING AUTHOR: Warren

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PA-11: Effectiveness and safety of clobetasol propionate 0.05% spray added on to regimens containing biologic agents for the treatment of moderate to severe plaque psoriasis

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BACKGROUND: Moderate to severe psoriasis often requires systemic treatment, but even biologic medications do not induce complete clearing in the majority of patients. Topical treatments are often used as adjuncts to systemic treatment. OBJECTIVE: To evaluate the effectiveness and tolerability of clobetasol propionate (CP) spray, 0.05% used either as monotherapy or added to ongoing (add-on) therapy. METHODS: A phase IV, multicenter, open-label trial was conducted to evaluate the effectiveness and safety of twice-daily CP 0.05% spray when added on to an existing stable regimen that included a biologic treatment (3 months duration) in 183 patients with moderate, severe, or very severe plaque psoriasis. RESULTS: By week 4, 78% of patients with moderate or severe disease and 66% of patients with very severe disease at baseline were clear or almost clear (P.<.0001). Worst skin tolerability response was assessed post-baseline and included erythema (28% mild, 6% moderate, 1% severe), peeling (29% mild, 7% moderate, 1% severe), dryness (35% mild, 9% moderate, 2% severe), and stinging (24% mild, 4% moderate, 1% severe). Telangiectasias and skin atrophy were reported in 1% of patients each at some point during the study (post-baseline). Pruritus was reported in 10% of patients, and folliculitis was reported in 1% of patients. A total of 10 patients experienced adverse events that were regarded as probably related to the study regimen, one of whom discontinued treatment. LIMITATIONS: This was a post hoc analysis, which would be confirmed using a prospective study. CONCLUSION: The addition of CP 0.05% spray to a stable regimen including a biologic resulted in a clear or almost clear status in the majority of patients and provides an option for additional control of psoriasis plaques when biologic agents as monotherapy are not as effective as physicians and patients require. CORRESPONDING AUTHOR: Ronald W. Gottschalk, MD, FRCP; Galderma Laboratories, L.P.; 14501 North Freeway, Fort Worth, TX 76177. E-mail: debi.stroud@galderma.com

PA-12: Effectiveness and safety of tavaborole, a novel boron-based molecule for the topical treatment of toenail onychomycosis: results from two phase 3 studies


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BACKGROUND: Onychomycosis is caused primarily by dermatophytes that invade the nail plate and nail bed causing nails to deform, discolor, thicken, split and separate from the nail bed. Limitations with oral treatment options include potential drug interactions and systemic adverse events. Currently approved topical agents are limited by their relatively lower efficacy and the need for adjunctive debridement. OBJECTIVE: Two double-blind, randomized, vehicle-controlled, phase 3 trials assessed the effectiveness and safety of tavaborole topical solution, 5% for the treatment of toenail onychomycosis. METHODS: Both studies enrolled adults with distal subungual onychomycosis affecting 20%-60% of the target great toenail. Study 301 enrolled patients in the United States and Mexico (N=594) and Study 302 enrolled patients in the United States and Canada (N=604). Patients were randomized 2:1 to apply tavaborole topical solution, 5% or vehicle solution to the affected toenails once daily for 48 weeks. Nail debridement was not permitted. The primary efficacy endpoint was complete cure defined as completely clear nail (no clinical evidence of onychomycosis) and negative mycology (negative KOH and fungal culture). Secondary endpoints included completely clear or almost clear nail, defined as <10% clinical involvement; negative mycology; and completely clear or almost clear nail with negative mycology. Primary and secondary endpoints were assessed at Week 52. Safety assessments included recording adverse events (AEs), local tolerability, clinical laboratory testing, physical examinations, vital signs, and electrocardiograms. RESULTS: The complete cure rates for tavaborole and vehicle in Study 301 were 6.5% and 0.5%, respectively (P.<.001), and 9.1% and 1.5% in Study 302, respectively (P.<.001). Negative mycology was achieved in 31.1% of patient treated with tavaborole vs 7.2% of vehicle-treated patients in Study 301 and 35.9% vs 12.2% of patients in Study 302 (for each, P.<.001). In both studies, the proportion of patients with completely clear or almost clear nail was superior with tavaborole: 26.1% vs 9.3% in Study 301; 27.5% vs 14.6% in Study 302 (for each, P.<.0001). A superior outcome was also observed for completely clear or almost clear nail with negative mycology with tavaborole treatment: 15.3% vs 1.5% in Study 301; 17.9% vs 3.9% for Study 302 (for each, P.<.001). In both phase 3 trials, tavaborole topical solution, 5% was well tolerated with no serious treatment-related AEs and a low rate of discontinuation resulting from AEs. CONCLUSION: Based on these data, the once-daily application of tavaborole topical solution, 5% appears to be a safe and effective treatment for toenail onychomycosis. CORRESPONDING AUTHOR: Lee T. Zane, MD; Anacor Pharmaceuticals, Inc.; 1020 East Meadow...
Onychomycosis is a common fungal infection of the nail. Oral treatment is generally required but may be limited by drug interactions and safety concerns. Efficacy rates of current topical treatments have been disappointing. Efinaconazole 10% solution is a new topical triazole antifungal developed for the treatment of onychomycosis. OBJECTIVE: To evaluate the efficacy of efinaconazole 10% solution vs vehicle in mild to moderate onychomycosis of the toenails. METHODS: Pooled analysis of 2 identical, multicenter, randomized, double-blind, vehicle-controlled studies in 1655 subjects aged 18-70 years with a clinical and mycological diagnosis of mild to moderate dermatophyte toenail onychomycosis (20%-50% clinical involvement). Subjects were randomized (3:1) to efinaconazole 10% solution or vehicle, once-daily for 48 Weeks, with 4-week post-treatment follow-up. All adverse events (AEs) occurring during the studies were recorded. A Fisher’s exact test was used to compare AEs occurring with frequencies of 1% or more. Localized skin reactions; changes in laboratory serum chemistry, hematology, and urinalysis parameters; vital sign measurements (systolic and diastolic blood pressure, heart rate, respiratory rate, and temperature); and changes in ECG findings were assessed throughout. RESULTS: AE rates with efinaconazole 10% solution and vehicle were similar (65.3% vs 59.8%, P=NS). They were generally mild (52.7%) or moderate (43.1%) in severity, and not related to study drug. There were no clinically meaningful changes from baseline in laboratory or vital sign measurements or ECG results for either treatment group. No serious AEs were related to the study drug and resolved with or without sequelae. CONCLUSION: Once daily efinaconazole 10% solution was well-tolerated and may be the first topical antifungal developed for the treatment of onychomycosis.
**PA-15: Efinaconazole 10% solution once-daily for mild to moderate onychomycosis: patient-reported outcomes in 1655 patients using a validated questionnaire**

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**BACKGROUND:** Onychomycosis is a common fungal infection of the nail. It can be distressing to many patients, associated with disability and pain, and may negatively affect a person’s wellbeing and self-esteem. In addition, psychological and social limitations may result from the reaction of others to visible nail disease. Efinaconazole 10% solution is a new topical triazole antifungal developed for the treatment of toenail onychomycosis. **OBJECTIVE:** To assess the benefits of efinaconazole 10% solution vs vehicle on patient-reported outcomes (PROs) in mild to moderate onychomycosis of the toenails. **METHODS:** The analysis pooled 2 identical, multicenter, randomized, double-blind, vehicle-controlled studies in 1655 subjects aged 18 to 70 years with a clinical and mycological diagnosis of mild to moderate dermatophyte toenail onychomycosis (20%-50% clinical involvement). Subjects were randomized (3:1) to efinaconazole 10% solution or vehicle, once daily for 48 weeks, with a 4-week post treatment follow-up. PROs were assessed using the validated OnyCOE-t questionnaire at baseline, week 24, and week 52. The OnyCOE-t includes a 7-point toenail symptom assessment, which comprises both symptom frequency and symptom bothersomeness scales; an 8-point appearance problems scale; a 7-point physical activities problems scale; a 1-point overall problem scale; a 7-point stigma scale; and a 3-point treatment satisfaction scale. Observed case analyses were performed. **RESULTS:** Mean change in scores from baseline to Week 52 were 26.5 (symptom frequency), 17.8 (symptom bothersomeness), 17.5 (physical activities problems), 22.6 (appearance problems), 28.0 (overall problem), and 9.2 (stigma) compared to 16.2 (P<.001), 10.9 (P<.001), 11.5 (P=.002), 14.9 (P<.001), 17.1 (P<.001), and 4.3 (P=.002) respectively with vehicle. In addition, the mean score for treatment satisfaction with efinaconazole 10% solution at week 52 was 71.6 compared to 41.6 with vehicle (P<.001). **CONCLUSION:** Once daily efinaconazole 10% solution provides clinically meaningful improvements in onychomycosis compared to vehicle. **CORRESPONDING AUTHOR:** Steve Feldman, MD, PhD; Departments of Dermatology, Pathology and Public Health Services; Wake Forest University School of Medicine; Winston-Salem, NC. E-mail: sfieldman@wfubmc.edu

**CONFLICTS:** R Pillai is an employee of Dow Pharmaceuticals, a division of Valeant Pharmaceuticals; J Olin and T Lin are employees of Medicis, a division of Valeant Pharmaceuticals.

**PA-16: Efinaconazole 10% solution: formulation development program for a new effective topical treatment for onychomycosis**

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1Dow Pharmaceuticals, a division of Valeant Pharmaceuticals, Petaluma, California; 2Medicis, a division of Valeant Pharmaceuticals, Bridgewater, New Jersey

**BACKGROUND:** Onychomycosis is a common fungal infection of the nail and nail bed. It is difficult to treat topically due to the barrier provided by highly keratinized nail tissue. The only approved topical product is a lacquer, which potentially limits the ability of the drug to reach the nail bed. This poster discusses the steps taken to develop an effective alcohol-based vehicle for efinaconazole. Efinaconazole is the first topical triazole to be specifically developed for onychomycosis and has been shown to have a broad-spectrum highly potent in vitro activity against all the common pathogens. **OBJECTIVE:** To formulate efinaconazole in a stable, non-lacquer vehicle that optimizes its access to the nail bed and provides a highly effective topical treatment for onychomycosis. **METHODS:** Several prototype formulations were developed using different solvents with good wetting properties (low surface tension) and high lipophilicity that maintain adequate solubility of efinaconazole after evaporation of volatile components. Prototypes were evaluated by conducting in vitro skin penetration studies and selected after assessment of their ability to penetrate human nails. A stability study was initiated to evaluate the physical and chemical stability. **RESULTS:** Delivery of efinaconazole across human skin ranged from 0.7% to 10.1% of the applied dose. The low surface tension formulation was best at penetrating through the human nail bed. As a result, it was selected for the Phase 2 clinical program. The formulation was studied under varied conditions of stress conditions resulting in a stability range from 99.7%-104.3% LC over 2 years at 25°C/60% RH in a bottle used in the clinic. **CONCLUSION:** Efinaconazole 10% solution is a stable, non-lacquer, topical antifungal with a unique combination of ingredients added to an alcohol based formulation to provide low surface tension and good wetting properties. This low surface tension provides effective penetration through the nail plate and is believed to access the nail bed by wicking into the space between the nail and nail plate. Efinaconazole 10% solution has been studied for the treatment of mild to moderate onychomycosis. The formulation development program succeeded in creating a clinically successful treatment. **CORRESPONDING AUTHOR:** Varsha Bhatt, PhD; Dow Pharmaceuticals; a division of Valeant Pharmaceuticals; Petaluma, CA 94954. E-mail: VBhatt@dowpharmsci.com

**CONFLICTS:** V Bhatt and R Pillai are employees of Dow Pharmaceuticals, a division of Valeant Pharmaceuticals; J Olin and N Soroudi are employees of Medicis, a division of Valeant Pharmaceuticals.
PA-17: First-Line Use of Calcipotriene/Betamethasone Dipropionate Combination Products for the Treatment of Plaque Psoriasis is Associated with Lower Health Care Utilization and Cost


BACKGROUND: Calcipotriene/betamethasone dipropionate combination topical products are an established treatment for patients with plaque psoriasis. In appropriate patients, using the combination products as first-line therapy after the psoriasis diagnosis might be beneficial. OBJECTIVE: This study investigated whether such use might lower the cost impact on health care budgets. METHODS: A retrospective study using Thomson Reuters MarketScan national claims data from 2006-2011 was performed to identify patients who received psoriasis medications following a psoriasis diagnosis (ICD-9 code 696.1x). Patients were continuously enrolled during 1-year pre- and post-index date periods. The 2 study cohorts were cohort A (patients treated with calcipotriene/betamethasone dipropionate combination products immediately post-diagnosis) and cohort B (patients treated with any other topical psoriasis medication immediately post-diagnosis). The frequency of office visits and total health care costs (includes pharmacy costs and costs of inpatient and outpatient services) during the 1-year post-index period were assessed. Multiple regression analyses adjusting for baseline demographic and clinical covariates, including a proxy for psoriasis severity, were performed. RESULTS: In total, 16,977 patients were identified in the 2 cohorts based on the topical medication prescribed (cohort A = 7307; cohort B = 9670). During the 1-year follow-up period, mean (± SD) total and psoriasis-related office visits were significantly lower in cohort A (13.36 ± 14.39; 2.79 ± 7.60) than cohort B (16.08 ± 16.68; 4.25 ± 10.23) (both P<.001). Mean total health care costs were less for cohort A ($7785.80 ± $15,255.60; median = $3411) than cohort B ($11,757.20 ± $19,747.60; median = $5595.80) (P<.001). In a generalized linear model adjusted for baseline covariates, cohort A had significantly lower costs than cohort B (β ± SE = 0.041 ± 0.017; P=.02). CONCLUSION: First-line treatment with calcipotriene/betamethasone dipropionate combination products after psoriasis diagnosis was associated with fewer office visits and lower total health care costs.

CONFLICTS: S Feldman reports personal fees from Leo Pharma, during the conduct of the study; grants and personal fees from Galderma, grants and personal fees from Amgen, grants and personal fees from AbbVie, grants and personal fees from Janssen, outside the submitted work.

PA-18: Imiquimod 2.5% and 3.75% for the treatment of actinic keratosis: assessment of efficacy in 479 randomized patients

Swanson N, Lin T, Jorizzo JL.

BACKGROUND: Approved imiquimod 5% cream regimen for actinic keratosis (AK) requires a long treatment course, limited to a small skin area. Daily dosing to reduce the length of treatment course was not well-tolerated. Frequent dosing with lower concentrations may provide a realistic option. OBJECTIVE: To assess the efficacy of more frequent dosing with a lower concentration (3.75% and 2.5%) imiquimod cream for AK treatment of the full face or balding scalp. METHODS: Two identical multicenter, randomized, double-blind, placebo controlled studies in adult subjects with 5 to 20 visible lesions, or palpable AKs in an area exceeding 25cm² on either the face or balding scalp. METHODS: Two identical multicenter, randomized, double-blind, placebo controlled studies in adult subjects with 5 to 20 visible lesions, or palpable AKs in an area exceeding 25cm² on either the face or balding scalp. RESULTS: Two identical multicenter, randomized, double-blind, placebo controlled studies in adult subjects with 5 to 20 visible lesions, or palpable AKs in an area exceeding 25cm² on either the face or balding scalp. Efficacy was assessed 8 weeks post treatment (End of Study Visit [EOS]). Primary efficacy was complete clearance at EOS. Secondary efficacy endpoints included rate of partial clearance at EOS (≥ 75% reduction in AK lesions) and median % decrease in lesion count. RESULTS: 479 subjects were enrolled (242 subjects Study 1 and 237 subjects Study 2). Complete clearance rates were 25.9% (Study 1), 45.6% (Study 2) and 23.5% (Study 1), 38.0% (Study 2) respectively in the 3.75% and 2.5% imiquimod groups compared to 2.5% (Study 1), 10.1% (Study 2) with vehicle (P<.001 vs vehicle). Partial clearance rates were 45.7% (Study 1), 73.4% (Study 2) and 42.0% (Study 1), 54.4% (Study 2) respectively in the 3.75% and 2.5% imiquimod groups at EOS compared to 18.8% (Study 1), 26.6% (Study 2) with vehicle (P<.001 vs vehicle). Median lesion count reductions from baseline were and 72.7% (Study 1), 90.9% (Study 2) and 60.0% (Study 1), 76.5% (Study 2) respectively for imiquimod 3.75% and 2.5% compared to 21.1% (Study 1), 30.0% (Study 2) with vehicle (P<.001 vs vehicle). The difference in complete clearance rates (imiquimod minus vehicle), partial clearance and median reduction in lesion counts was 23.4% and 21.5% (Study 1) and 35.5% and 27.9% (Study 2), 26.9% and 23.2% (Study 1) and 46.8% and 27.8% (Study 2), and 51.6% and 38.9% (Study 1) and 60.9% and 46.5% (Study 2), respectively. CONCLUSION: In 2 well-controlled Phase 3 studies, both imiquimod 2.5% and 3.75% creams were more effective than vehicle cream when administered daily as a 2-week on/off/on regimen to treat AK.
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CONFLICTS: N Swanson and J Jorizzo were investigators for Medicis, a division of Valeant Pharmaceuticals. N Swanson was a speaker for LEO Pharma Inc, and consultant for LEO Pharma Inc and Medicis. J Jorizzo was an advisor for Amgen, LEO Pharma Inc, and Warner Chilcott. T Lin is an employee of Medicis, a division of Valeant Pharmaceuticals.

PA-19: Imiquimod 2.5% and 3.75% for the treatment of actinic keratosis: assessment of safety in 479 randomized patients

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BACKGROUND: The approved imiquimod 5% cream regimen for treating actinic keratosis (AK) requires a long treatment course that is limited to a small area of the skin. Unfortunately, daily dosing to reduce the length of treatment course was not well-tolerated. More frequent dosing with lower concentrations may be a more realistic option. OBJECTIVE: To assess the safety and tolerability of more frequent dosing with a lower concentration (3.75% and 2.5%) imiquimod cream for the treatment of the full face or balding scalp. METHODS: Two identical multicenter, randomized, double-blind, placebo controlled studies in adult subjects with 5 to 20 visible lesions, or palpable AKs in an area exceeding 25 cm² on either the face or balding scalp, randomized to imiquimod 3.75%, 2.5%, or vehicle cream (1:1:1). Up to 2 packets (250 mg each) were applied per dose once daily for two 2-week treatment cycles, separated by a 2-week, no-treatment interval. Safety assessments included visual assessment of local skin reaction (LSR), number and duration of study treatment rest periods required due to intolerable LSRs, adverse events (AEs) and clinical laboratory tests. RESULTS: Most AEs were mild or moderate in intensity and unrelated to treatment. There were few treatment-related discontinuations. Two subjects in the imiquimod groups and 3 in the vehicle cream group discontinued due to AEs, only one of which (a moderate headache reported in the vehicle group) was considered treatment-related. Serious adverse events (SAEs) were reported in 12 subjects. Only one was considered treatment-related (severe diarrhea with 3.75% imiquimod). Reported LSRs (erythema being the most common) increased in a dose-dependent manner. The LSR sum AUCs for the 2.5% and 3.75% imiquimod treatment groups were significantly greater than for vehicle. Rest periods were taken by 5 (6.2%, Study 1) and 6 (7.6%, Study 2) in the imiquimod 2.5% groups, and 7 (8.6%, Study 1) and 10 (12.7%, Study 2) in the imiquimod 3.75% groups, and none of the subjects in the vehicle group. CONCLUSION: In two well-controlled Phase 3 studies, both imiquimod 2.5% and 3.75% creams were well tolerated when administered daily as a 2-week on/off/on regimen to treat AK.

PA-20: Imiquimod 2.5% and 3.75% for the treatment of external genital warts: assessment of efficacy in 981 randomized patients

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BACKGROUND: The approved imiquimod 5% cream regimen for treating external genital warts (EGW) requires a long treatment. Unfortunately, daily dosing to reduce the length of treatment course resulted in a greater incidence and severity of local adverse events (AEs) without an improvement in efficacy. OBJECTIVE: To assess the efficacy of more frequent dosing with lower concentration (3.75% and 2.5%) imiquimod cream in treating EGW. METHODS: Two identical multicenter, randomized, double-blind, placebo controlled studies. Subjects (≥12 years old) with 2-30 EGWs and total wart area of ≥10 mm² randomized to imiquimod 3.75%, imiquimod 2.5%, or placebo (2:2:1) once daily until complete clearance or a maximum of 8 weeks (end of treatment [EOT]), with a follow-up period of up to 8 weeks (end of study [EOS]) for subjects who did not achieve complete clearance by EOT; and a 12-week observational follow-up period in subjects with complete clearance at EOS. Primary efficacy endpoint was complete clearance (% subjects at EOS with zero EGW count). Secondary efficacy endpoints were rate of partial clearance (≥ 75% reduction in EGW count), change in wart count, and 12-week sustained clearance rate. RESULTS: 981 subjects were enrolled (470 subjects in Study 1 and 511 subjects in Study 2). Complete clearance rates were 27.2% (Study 1), 29.4% (Study 2) and 19.1% (Study 1), 24.8% (Study 2) respectively in the 3.75% and 2.5% imiquimod groups compared to 10.3% (Study 1), 8.6% (Study 2) with placebo (P<.001 imiquimod 3.75% vs placebo). Partial clearance rates were 37.9% (Study 1), 38.7% (Study 2) and 27.0% (Study 1), 31.2% (Study 2) respectively compared to 13.4% (Study 1), 10.5% (Study 2) with placebo (P<.001 imiquimod 3.75% vs placebo). Mean lesion count reductions from baseline were 45.8% (Study 1), 40.9% (Study 2) and 26.6% (Study 1), 37.7% (Study 2) respectively for imiquimod 3.75% and 2.5% compared to 13.4% (both Study 1 and 2) for placebo (P<.001 versus placebo). 75.5% (Study 1) and 64.2%
(Study 2) of subjects in the imiquimod 3.75% group achieved complete clearance at EOS that was sustained throughout the 12-week follow-up period, compared to 48.4% (Study 1) and 67.4% (Study 2) in the imiquimod 2.5% group. CONCLUSION: In 2 well-controlled Phase 3 studies, both imiquimod 2.5% and 3.75% creams were more effective than placebo when administered daily for up to 8 weeks to treat EGW. Imiquimod was most effective in terms of complete clearance and partial clearance rates. CORRESPONDING AUTHOR: Anita Nelson, MD; Department of Obstetrics & Gynecology; David Geffen School of Medicine; University of California; Los Angeles, CA 90095. E-mail: anitanelson@earthlink.net CONFLICTS: S Tyring was an investigator for Medicis, a division of Valeant Pharmaceuticals. S Tyring, A Nelson, and K Ault were consultants and/or advisory board members for Medicis. T Lin is an employee of Medicis.

PA-21: Imiquimod 2.5% and 3.75% for the treatment of external genital warts: assessment of safety in 981 randomized patients

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BACKGROUND: The approved imiquimod 5% cream regimen for treating external genital warts (EGW) requires a long treatment. Unfortunately, daily dosing to reduce the length of treatment course resulted in a greater incidence and severity of local adverse events (AEs) without an improvement in efficacy. OBJECTIVE: To assess the safety and tolerability of more frequent dosing with lower concentration (3.75% and 2.5%) imiquimod cream in treating EGW. METHODS: Two identical multicenter, randomized, double-blind, placebo controlled studies. Subjects (≥12 years old) with 2-30 EGWs and total wart area of ≥10 mm2 randomized to imiquimod 3.75%, imiquimod 2.5%, or placebo (2:2:1) once daily until complete clearance or a maximum of 8 weeks (end of treatment, EOT), with a follow-up period of up to 8 weeks (end of study, EOS) for subjects who did not achieve complete clearance by EOT; 12-week observational follow-up period in subjects with complete clearance by EOS. Safety assessments included visual assessment of local skin reaction (LSR), number and duration of study treatment rest periods required due to intolerant LSRs, adverse events (AEs) and clinical laboratory tests. RESULTS: Most AEs were mild or moderate. The most frequently reported AEs were application site reactions observed in the active treatment groups. Treatment-emergent AEs that lead to study discontinuation were reported in 7, 10 and 1 subject in the imiquimod 3.75%, imiquimod 2.5%, and placebo groups. Eight subjects in the imiquimod groups withdrew because of application site reactions, considered related or possibly related to treatment. Treatment with either imiquimod strength resulted in greater increases in LSRs compared with the placebo. Erythema was reported with the greatest frequency and greatest mean intensity in all treatment groups. For both active creams, the number and severity of LSRs decreased rapidly after the completion of treatment. Rest periods were taken by 126, 104, and 4 subjects in the 3.75% imiquimod, 2.5% imiquimod, and placebo groups, respectively. The frequency, duration, and number of dosing days prior to the rest period were similar in the active treatment groups and lower in the placebo group. There was no evidence of clinically meaningful trends in vital sign measurements or clinical laboratory measurements. CONCLUSION: In 2 well-controlled Phase 3 studies, both imiquimod 2.5% and 3.75% creams were well tolerated when administered daily for up to 8 weeks to treat EGW. CORRESPONDING AUTHOR: Gary Goldenberg, MD; Mount Sinai School of Medicine; Department of Dermatology; New York, NY 10029. E-mail: garygoldenbergmd@gmail.com CONFLICTS: J Del Rosso was a consultant, speaker, and/or researcher for Allergan, Bayer, Eisai, Galderma, Medicis, a division of Valeant Pharmaceuticals, Onset Dermatologics, Obagi Medical Products, PharmaDerm, Primus, Promius, Ranbaxy, Triabella, Unilever, and Warner-Chilcott; T Lin is an employee of Medicis; A Nelson was a consultant to Medicis.

PA-22: In vitro nail penetration study with human nails demonstrates penetration of tavaborole topical solution, 5% through nail polish

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BACKGROUND: Onychomycosis causes nails to become thickened and discolored, often leading to social embarrassment. Individuals may wish to use nail polish to mask the appearance of infected nails due to onychomycosis. To be effective, topical antifungal medications must be able to penetrate through the nail plate and into the nail bed. Tavaborole topical solution, 5% for the treatment of onychomycosis has demonstrated the ability to readily penetrate the nail plate. OBJECTIVE: To evaluate the penetration of tavaborole topical solution, 5% through nail polish on fingernails obtained from human female cadavers. METHODS: Five fingernails from 4 donors (N=20) were divided into 2 treatment groups. Two nails per donor received one coat of a commercial brand of nail polish. Another two nails per donor received no nail polish. One nail from each donor served as a non-dosed control. Tavaborole topical solution, 5% was applied to each nail (except the non-dosed control) once daily for 20 consecutive days using a positive placement pipette calibrated to deliver 12.5 uL/cm2 of solution. Using the Franz Finite dose model, drug penetration was measured by monitoring its rate of appearance in the receptor solution (phosphate buffered saline) bathing the inner surface of the nail. Aliquots of the receptor solution samples were collected over the course of the study and analyzed for the presence of tavaborole using a qualified liquid chromatography-tandem mass spectrometry (LC/MS/MS) method. RESULTS: The mean (SD) cumulative penetration of tavaborole in the treatment group with nail polish was 3526 (1433) ug/cm2 compared to 2661 (1319) ug/cm2 in
the treatment group with no nail polish. The penetration of tavaborole topical solution, 5% through nails with nail polish was not statistically different from penetration through nails without nail polish. LIMITATIONS: This was an in vitro study. CONCLUSION: These results demonstrate tavaborole topical solution, 5% was able to penetrate through one coat of a commercial brand of nail polish using an ex vivo human female fingernail model. CORRESPONDING AUTHOR: Lee T. Zane, MD, Anacor Pharmaceuticals, Inc.; 1020 East Meadow Circle; Palo Alto, CA 94303. E-mail: LZane@anacor.com

PA-24: Korean general population-based health risk assessment (HRA) for alopecia

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BACKGROUND: Androgenetic alopecia (AGA) is a common skin disease with aging and increasing among younger ages in Asia. Although this is thought to be a non-modifiable disease due to the genetic factor, there are many modifiable factors we can manage. OBJECTIVE: To make an innovative tool to assess the risk of AGA based on the Korean general population.

METHODS: For the reference, we selected articles by specific standard. Among the related studies that have shown odd ratio (OR), risk ratio (RR) or hazard ratio (HR), domestic was preferred. If the result did not have any sense in a domestic study, then we selected meaningful overseas articles showing similar trends and removed the OR from the domestic study. With respect to the risk factor, we excluded the risk factor if there was a large gap in the result between domestic and overseas studies. RESULTS: We selected age, family history, alcohol intake, weight circumference, high blood pressure, high-density lipoprotein (HDL), ultraviolet (UV) exposure/protection for the risk factor. Additionally we included diabetes mellitus, number of childbirths, breast feeding period, oral contraceptive use for the risk factor. Among the factors, the OR of childbirths, breast feeding period, oral contraceptive use for the risk factor were 1.37 (same in women), 1.14 (1.27 in women), 5.44 in men and 1.64 in women. And that of obesity was 3.7 (same in women), 2.9 (1.5 in women), 2.3 (1 in women). We can quantify the risk of alopecia and hope to manage this by correcting the modifiable factors. Further, this tool is expected to be used in health promotion centers.

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PA-25: Maximal use systemic exposure (MUSE) study evaluating AN2728, a novel boron-based small molecule, for the treatment of subjects 2 to 17 years old with mild to moderate atopic dermatitis

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BACKGROUND: AN2728 is a novel boron-based compound that inhibits phosphodiesterase-4 activity and reduces the production of pro-inflammatory cytokines that may be associated with atopic dermatitis (AD). OBJECTIVE: The objective of this open-label, maximal-use study was to evaluate the systemic exposure, pharmacokinetics, and safety of AN2728 topical ointment, 2% applied twice daily for 28 days for the treatment of AD in children and adolescents. METHODS: The study enrolled 34 subjects with mild to moderate AD, defined as a score of 2 (mild) or 3 (moderate) on the 5-point investigator’s Static Global Assessment (ISGA) scale in 3 patient cohorts based on age and minimum percent of treatable body surface area (%BSA) affected: 2-5 years old (>35%), 6-11 years old (>35%) and 12-17 years old (>25%). During the first 8 days when pharmacokinetic assessments were performed, subjects were dosed in the clinic; dosing was performed at home thereafter. Disease severity was measured using ISGA (0, clear to 4, severe), signs/symptoms score (0, none to 3, severe) and %BSA affected. RESULTS: At Day 29, 65% of subjects achieved ISGA scores of clear or almost clear and 47% of subjects achieved scores of clear or almost clear with a >2-grade improvement from baseline. Marked reductions from baseline were observed across all the individual signs and symptoms of AD (pruritus, erythema, lichenification, excoration and exudation) throughout the treatment period. Notably, mean pruritus scores improved by approximately 60% from baseline as early as 5 days into treatment. The mean %BSA affected decreased by an average of 78% across all subjects after 4 weeks of treatment. The most common treatment-related adverse events were application site reactions (occurring in 12 subjects) which generally were mild or moderate in severity and resolved spontaneously. One patient withdrew from the study due to application site pain. Pharmacokinetic results demonstrated low blood levels of AN2728 similar to those previously observed in adults after adjusting for %BSA treated. LIMITATIONS: This was an open-label study. CONCLUSION: These results generated under maximal-use conditions suggest that AN2728 topical ointment, 2% may be safe and effective in subjects 2 years of age and older with mild to moderate AD.

PA-26: Novel topical cream delivers safe and effective alternative to traditional psoriasis phototherapy

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BACKGROUND: In today’s environment of shrinking reimbursement and coverage for many health care procedures, phototherapy for psoriasis has experienced a major decline. Once hailed as the cornerstone of psoriasis therapy, the increasing cost and demanding treatment regimen has resulted in poor compliance, limiting access to this safe and effective mode of treatment. OBJECTIVE: Here we report on the development of a topical cream that selectively filters solar radiation to deliver narrow-band UVB for the treatment of psoriasis. This cream was evaluated in a pilot clinical study. METHODS: We performed a double-blind placebo-controlled study of 15 patients. The patients were randomly assigned to either the treatment arm or the placebo arm. The placebo was a broad-spectrum sunscreen with an SPF of 2. The SPF of the placebo was chosen to represent the theoretically modeled SPF of the novel cream derived from UV absorption data. During each treatment session, patients were exposed to natural sunlight outside the principal investigator’s clinic. The duration of each session was determined by a minimal erythemal dose (MED) chart taking into account each patient’s skin type and the UV index at the time of treatment. During treatment, each patient applied an arm-assigned cream (drug or placebo) to the treated lesion area and a broadband SPF 50 sunscreen to the non-lesion exposed areas. Global photography of each treated lesion was taken at the beginning and end of the treatment sessions. The lesion surface area changes were derived by blinded photography assessment. RESULTS: After an average of 38 sessions, all patients in the treatment arm responded to therapy. In particular, 43% of the treatment group experienced complete clearance and the remainder experienced at a minimum 50% lesion clearance. In contrast, none of the patients in the placebo arm experienced more than 20% lesion clearance. CONCLUSION: Our preliminary results demonstrate that the novel topical cream could provide a safe, effective, and convenient alternative to artificial light phototherapy.

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CONFLICTS: Applied Biology, Inc. developed Photocil, the drug evaluated in this clinical trial.
**PA-27**: Overall tolerability of adapalene/benzoyl peroxide from a pooled data analysis

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**BACKGROUND**: Adapalene-benzoyl peroxide (A-BPO) (stabilized in the Simulgel vehicle) gel 0.1%/2.5% has demonstrated effectiveness in the treatment of acne vulgaris in several clinical trials. **OBJECTIVE**: To further describe the tolerability of this treatment, data were analyzed from several clinical studies that investigated the effectiveness and safety of A-BPO gel 0.1%/2.5%. **METHODS**: Data from 14 studies were pooled to evaluate the tolerability of A-BPO gel 0.1%/2.5% gel among acne subjects. A total of 2,358 subjects between 9 years and 61 years old were treated with A-BPO gel 0.1%/2.5%. Frequency, percentages, and worst postbaseline scores were summarized for dryness, erythema, scaling, and stinging/burning. **RESULTS**: Most subjects experienced a worst postbaseline score of none or mild, 83.2% for dryness, 78.6% for erythema, 86.1% for scaling, and 76.8% for stinging/burning. Two percent or fewer subjects had a severe score for dryness, erythema, and scaling, and less than 5% of subjects had a severe score for stinging/burning. Fewer than 2% of subjects discontinued due to an adverse event. Even subjects with moderate and severe scores for the tolerability endpoints had improved IGA scores from baseline to week 4. **LIMITATIONS**: This was a post hoc analysis using data from different studies. **CONCLUSION**: In this large pooled analysis, A-BPO gel 0.1%/2.5% was well tolerated and provided benefit even in subjects who had a less favorable tolerability profile. **KEYWORDS**: Acne vulgaris, adapalene, benzoyl peroxide, tolerability

**PA-28**: Patient-reported effectiveness for calcipotriene and etamethasone dipropionate suspension and ointment formulations in psoriasis vulgaris: 4- and 12-week interim results from PRO-long

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**BACKGROUND**: PRO-long is a long-term, 52-week study of calcipotriol and betamethasone dipropionate (CBD) suspension and ointment formulations for the treatment of psoriasis vulgaris. **OBJECTIVE**: To describe patients’ perspectives on the 2 formulations, in terms of adherence behavior, treatment satisfaction, disease severity, and health-related quality of life, during psoriasis management in daily clinical practice. **METHODS**: This multicenter, prospective, observational, 52-week, cohort study recruited 275 patients who were prescribed CBD suspension or CBD ointment for the long-term management of psoriasis. The primary end point, difference in effectiveness between CBD suspension and CBD ointment, was assessed by the number of patients with controlled (mild or very mild) disease, based on the Patient Global Assessment (PaGA) questionnaire, at week 12. In addition, questionnaires were used to assess adherence behavior, treatment satisfaction (9-item Treatment Satisfaction Questionnaire for Medication [TSQM-9]) and health-related quality of life (SkinQ-29). Here we report interim results collected at 4 and 12 weeks. **RESULTS**: Data from 156 patients (39.7% female, 60.3% male), median age 48 (11–77) years, were analyzed. At baseline, the percentage of patients (mean [SD]), with controlled disease was 30% (44.8%) in the CBD ointment group (n=67) and 45% (50.6%) in the CBD suspension group (n=89). At week 4 (secondary end point) and week 12 (primary end point), there were no statistically significant differences in effectiveness between the groups at these time points, respectively: CBD suspension (67% [64%] and 64% [72%]) and CBD ointment (38% [57%] and 44% [66%]). Significantly more patients had controlled disease by weeks 4 and 12, compared with baseline, in both treatment cohorts: CBD suspension at week 4 (P=0.01) and week 12 (P=.0003); CBD ointment at week 4 (P=.03) and week 12 (P=.002). Although the majority of patients in both cohorts reported that application was “never” or “rarely” too great a burden, 10.2% of ointment-treated patients considered it “often” or “always” too great a burden, compared with 3.9% of suspension-treated patients. The proportion of patients spending less than 5 minutes per day applying the treatments was 85.7% in the suspension-treated group and 71.2% in the ointment-treated group. Treatment satisfaction was higher for patients treated with suspension compared with ointment across all TSQM-9 domains at weeks 4 and 12, particularly in the items measuring ease, based on the Patient Global Assessment (PaGA) questionnaire, at week 12. In addition, questionnaires were used to assess adherence behavior, treatment satisfaction (9-item Treatment Satisfaction Questionnaire for Medication [TSQM-9]) and health-related quality of life (SkinQ-29). Here we report interim results collected at 4 and 12 weeks. **CONCLUSION**: This first real-life study, comparing CBD suspension and CBD ointment, revealed no significant differences in patient-reported effectiveness between the 2 treatments. In single items of the treatment satisfaction and adherence questionnaires, patients showed a preference for the gel and considered it convenient, easy to use, and fast to apply. **CORRESPONDING AUTHOR**: J. Lambert, Department of Dermatology, Ghent University Hospital, Belgium. E-mail: jo.lambert@ugent.be

**PA-29**: Predicting improvement in signs and symptoms of plaque psoriasis after 1 week of treatment with clobetasol propionate 0.05% spray

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BACKGROUND: Early response to topical therapy, especially for pruritus, may be one important motivator to ensure adherence of patients to their full course of therapy. OBJECTIVE: Clobetasol propionate 0.05% (CP) spray has demonstrated response in clinical trials after 1 week of therapy. METHODS: Two phase 3, multicenter, randomized, double-blind, vehicle-controlled, parallel-group, comparative studies; men or women, 18 years of age and older, with plaque psoriasis affecting at least 2% body surface area; overall disease severity (ODS) of 3 (moderate) or 4 (severe/very severe); Endpoints: Primary efficacy endpoint: ODS on a 5 point scale (0 = clear, 4 = severe/very severe); Secondary efficacy endpoints: pruritus, plaque elevation, erythema, and scaling on 5 point scales (0 = clear, 4 = severe/very severe); Data modeled using a generalized linear model with the week 4 result as the dependent variable and the week 1 result and treatment as independent variables RESULTS: Subjects on CP spray whose week 1 ODS or pruritus score was at most mild were treatment successes (clear or almost clear) at week 4. A negligible number of vehicle-treated patients demonstrated a response at both week 1 and week 4 for either ODS or pruritus. Pruritus and disease severity responses to CP spray at 1 week predicted treatment success in both pruritus and the overall disease severity at 4 weeks. LIMITATIONS: This was a post hoc analysis, which would be confirmed using a prospective study CONCLUSION: Pruritus and disease severity responses to CP spray at 1 week predicted treatment success in both pruritus and the overall disease severity at 4 weeks.

PA-30: Racial differences in clinical characteristics, perceptions, and behaviors among adult females with acne vulgaris

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BACKGROUND: Acne vulgaris is a frequently encountered externally visible skin disease in dermatology. Although acne has traditionally been treated homogeneously across skin types, acne characteristics can vary across racial and ethnic backgrounds and special considerations may be needed in treating various colors of skin. A broader understanding of racial/ethnic variations of acne characteristics in adult females will help to improve treatment outcomes. OBJECTIVE: To compare racial differences in acne onset, acne severity, and facial acne location in adult female acne (AFA). METHODS: A cross-sectional, web-based survey was administered in 2011 (cohort 1) and 2013 (cohort 2) to a diverse sample of United States adult females (25–45 years) with acne (≥25 visible facial pimples). Survey outcomes included sociodemographic and clinical characteristics, perceptions, coping behaviors, and special needs for acne care and treatment (skin of color only). The current study combines data from both cohorts to explore differences in acne characteristics between White and non-White adult females. Descriptive statistics summarized results by racial group; Student’s t-test and chi-square analyses evaluated racial differences (White vs non-White). RESULTS: A total of 312 females with acne completed the survey (mean age 35±6 years), comprised of White (n=107) and non-White (n=205; Black [n=96], Hispanic [n=55], Asian [n=31], and Other [n=23]). Mean age of acne onset (White 14.8±5 years vs non-White 17.1±8 years, P<.05) and concern for acne (16.6±7 vs 19.2±9 years, P<.05) occurred earlier in White than non-White females. The most frequent concerns among both Whites and Non-Whites were both pimples and postinflammatory hyperpigmentation (PIH, 63.6% and 67.8%). Facial acne presented most often on the cheeks (30.8 %) and chin (28.0%) for Whites and the cheeks (56.1%) and forehead (18.0%) for non-White females. Beyond the face, Whites experienced more acne on the chest (46.7% vs 30.2%, P<.01) and other body parts (21.5% vs 12.7%, P<.05) than non-White females. White females more often reported at least a moderate amount of redness (in the past 4 weeks) from facial acne (74.8% vs 57.5%, P<.05) compared to non-White females; however they less frequently reported at least a moderate amount of scarring (54.2% vs 68.3%, P<.05) and dark marks (48.7% vs 68.3%, P<.01) in the past 4 weeks than non-Whites. LIMITATIONS: Limitations included potential selection bias due to web-based data collection methodology; use of targeted sampling, use of self-reported clinical information, and potential response bias due to current acne severity (overall acne severity may have differed from time of screening). Enrollment was also limited to females who self-reported ≥25 visible facial lesions, excluding milder cases and limiting the generalizability of conclusions to all forms of AFA severity. CONCLUSION: Self-reported clinical characteristics of facial AFA varied with race. Onset of acne in White females began significantly earlier and was considered more troublesome than for non-White females. Non-Whites expressed more concern about PIH than Whites. These results may help inform clinicians about racial differences in clinical presentation of facial AFA, increase awareness of specific needs of non-White females, and guide treatment recommendations. CORRESPONDING AUTHOR: David A. Rodriguez; Dermatology Associates and Research; 1301 Ponce de Leon Blvd; Coral Gables, FL 33134. E-mail: darmd1@aol.com CONFLICTS: Declaration of funding: This study was sponsored by Allergan, Inc.; Declaration of financial/other relationships: D Rodriguez. has nothing to disclose. M Rendon has an industry relationship with Allergan,
PA-31: Safety and efficacy of AN2728 topical ointment, 2% and 0.5%, in a phase 2 dose-ranging study of adolescents with mild to moderate atopic dermatitis

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BACKGROUND: AN2728 is a novel oxaborole compound and phosphodiesterase-4 inhibitor with anti-inflammatory activity. OBJECTIVE: A clinical dose-ranging study was conducted to determine the safety and efficacy of AN2728 topical ointment, 2% and 0.5%, administered once daily (QD) or twice daily (BID), in the treatment of mild to moderate atopic dermatitis (AD) in adolescents. METHODS: This multi-center, randomized, double-blind, bilateral, dose-ranging, phase 2 study enrolled 86 patients (40% male) aged 12-17 years with AD involving up to 35% of their body surface area. Enrolled patients had 2 target lesions of similar severity based on AD severity index (ADSI) score of 6-12, a maximum 1-point difference in ADSI score between the 2 lesions, and an erythema subscore of at least 2 (moderate). The index comprises the sum of scores ranging from 0 (none) to 3 (severe) for erythema, pruritus, excudation, excoriation, and lichenification. Patients were randomly assigned to a QD or BID treatment frequency. In addition, patients treated one target lesion with AN2728 topical ointment, 2% and the other with AN2728 topical ointment, 0.5%. Patients were evaluated on days 1, 8, 15, 22, and 29. Disease severity was determined based on the ADSI score on days 8, 15, 22, and 29. The primary endpoint was the change from baseline in ADSI score. RESULTS: AN2728 topical ointment, 2% and 0.5%, were found to be generally safe and well-tolerated. No serious adverse events (AEs) were reported, and no treatment discontinuation occurred due to AEs. Application site symptoms were uncommon. Based on improved ADSI scores relative to baseline, a clear dose-response was seen across the 4 dosing regimens. The greatest improvement in ADSI score was noted with treatment with AN2728 topical ointment, 2% BID, which yielded a 71% improvement in ADSI score from baseline after 28 days, with 62% of lesions in this treatment group achieving total or partial clearance. This treatment group also demonstrated the greatest improvement across all 5 signs and symptoms of AD after 28 days, including a notable 79% reduction in pruritus severity. CONCLUSION: Of the 4 dosing regimens examined in this Phase 2 study of adolescents with AD, AN2728 topical ointment, 2% BID produced the greatest improvements in disease severity and was generally safe and well tolerated. CORRESPONDING AUTHOR: Lee T. Zane, MD; Anacor Pharmaceuticals, Inc.; 1020 East Meadow Circle; Palo Alto, CA 94303. E-mail: LZane@anacor.com CONFLICTS: L Zane reports this study was sponsored by Anacor Pharmaceuticals, Inc., and that he and M Hughes are employees of the company.

PA-32: The Use of a Tablet-based Rating Scale in Subjects with Plaque Psoriasis Treated with Clobetasol Propionate 0.05% Spray

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BACKGROUND: Store-and-forward teledermatology is an emerging technology with the potential to initiate a paradigm shift in how patients and health care providers (HCPs) interact. Ubiquitous devices, such as tablets and smartphones, may provide a simple medium to facilitate such interactions. OBJECTIVE: A pilot study was conducted to investigate the use of a tablet based numeric rating scale to track improvement of a plaque psoriasis target lesion treated with clobetasol propionate 0.05% spray. METHODS: Twenty-eight subjects aged 18 years and older with plaque psoriasis affecting up to 20% body surface area were enrolled for the study. Subjects applied CPS twice-daily to a target lesion for 15 days. Target lesion severity was assessed using the target lesion numeric rating scale (TL-NRS; 0 [none] to 10 [very severe]) and effectiveness scores were assessed on a scale of 0 (none) to 4 (very severe) including erythema/redness, plaque elevation/thickness, scaling, and pruritus/itching assessed on a scale of 0 (none) to 3 (severe). Subjects were asked a treatment satisfaction questionnaire during the study. RESULTS: Investigator and subject reported TL-NRS scores and effectiveness scores improved from baseline to day 15. Subjects indicated a high satisfaction with CPS. Four related adverse events were reported during the study and were all mild in severity. Very few technological failures were reported during the study. LIMITATIONS: This was a small pilot study that was not powered. A larger, powered study would confirm the results and the utility of this methodology. CONCLUSION: Taken together, the results of this study indicate that CPS is a safe and effective treatment for plaque psoriasis and support the use of a tablet-based rating scale to measure and track disease progression. CORRESPONDING AUTHOR: Warren Winkelman, MD; Galderma Laboratories, L.P.; 14501 North Freeway, Fort Worth, TX 76177. E-mail: warren.winkelman@galderma.com CONFLICTS: W Winkelman is an employee of Galderma Laboratories, L.P.

PA-33: Efficacy of sequential treatment with ingenol mebutate gel 0.015%, following cryosurgery for actinic keratosis on the face and scalp

Inc. C Burk is a consultant for Allergan, Inc. A Kawata and T Wilcox are employees of Evidera. The research and medical writing conducted by Evidera for this abstract were funded by Allergan, Inc. A Degbo and S Daniels are employees of Allergan Inc. W Roberts has industry relationships with Allergan, L’Oreal, La Roche Posay, MelaScience, Neostrata, Theraplex, and Top MD.
BACKGROUND: Cryosurgery effectively treats individual lesions of actinic keratosis (AK), yet recurrence rates are high, and the treatment does not address field cancerization of perilesional skin. OBJECTIVE: To compare complete clearance of AK lesions using cryotherapy followed by field treatment with ingenol mebutate (IngMeb) compared with cryotherapy and vehicle gel. The 12-month efficacy results from our study evaluating sequential treatment of AKs on the face and scalp with cryosurgery followed by IngMeb 0.015% gel vs cryosurgery and vehicle gel are presented. METHODS: This was a phase 3, multicenter, randomized, two-arm, parallel-group, double-blind, vehicle-controlled, 12-month study (NCT01541553). Patients with 4–8 clinically, typical, and discrete AKs within a contiguous 25-cm² treatment area on the face or scalp were enrolled, and received liquid nitrogen cryosurgery to all visible AKs. Patients were randomized to field treatment with IngMeb 0.015% gel or vehicle gel once daily for 3 consecutive days. Three weeks after cryosurgery, field treatment was applied to patients in both groups. The primary endpoint was complete clearance of AKs in the treatment area at week 11. Secondary endpoints were percentage reduction in the total number of AKs and partial clearance rate (≥75%) of AKs across the period from week 11 to 12 months. Patients who withdrew early were classified as non-responders. RESULTS: A total of 329 patients (80.5% with face and 19.5% with scalp lesions) were randomized to IngMeb 0.015% gel (n=167) or vehicle (n=162) gel following cryosurgery. These patients were all white, predominantly male (82.4%), and had a median age of 67 years (range 34–89); most had Fitzpatrick skin type I (15.2%) or II (48%). In total, 92% completed 11 weeks and 88% concluded the 12-month period. Complete clearance rates were greater with IngMeb compared with vehicle for all lesions at 11 weeks (60.5% vs 49.4%; P=.04) and 12 months (30.5% vs 18.5%; P=.01). The relative complete AK clearance achieved by 11 weeks increased at 12 months in the IngMeb-treated field, while in the vehicle group, lesions, only 38.9% of patients experienced new emerging lesions in the IngMeb-treated field, while in the vehicle group, 51.9% of patients had new lesions emerging from previously not visible subclinical lesions (P=.01). The mean percent reduction of AKs at 12 months was significantly higher with IngMeb for all lesions (59.5% vs 44.4%; P=.004) than with vehicle.

PA-34: Role of sonic hedgehog pathway in basal cell carcinoma development among central European Caucasians

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BACKGROUND: A recent increase in the frequency of non-melanoma skin cancers (NMSC), which include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), has been observed in the United States, Europe, and Australia. Despite low mortality, NMSC is a major medical, social, and economic problem. Sonic hedgehog (Shh) pathway impairment plays a key role in BCC pathogenesis, which is the most frequent skin tumor among Caucasians, estimated between 18%-40%. In our previous studies the role of SHH, PTCH and SMO genes polymorphisms were determined in 142 BCC cases and 142 controls of Polish origin. OBJECTIVE: The purpose of the study was to clarify the role of SHH signaling in skin BCC, the expression of SHH, PTCH1 and SMO. METHODS: We assessed single nucleotide polymorphisms with the use of the PCR-RFLP method. The expression of SHH, PTCH1 and SMO were examined in 42 sporadic nodular skin basal cell carcinoma and 15 control healthy skin by Western blot. RESULTS: All the biopsies revealed the expression of the SHH, PTCH1 and SMO proteins. Their levels were significantly higher in BCC specimens than in the control skin (median 3.4x105 IDV vs median 3.1x105 IDV for SHH; median 2.5x105 IDV vs median 2.0x105 IDV for PTCH1; and median 2.9x105 IDV vs median 1.5x105 IDV for SMO; P<.05 for all comparisons). Additionally when the level of expression of the examined proteins was correlated with the selected polymorphisms, the BCC patients with the AT genotype SHH rs10489404 349T/C gene polymorphism had significantly higher expression of SHH compared with TT carriers (median 3.69x105 IDV vs 3.25x105 IDV; P<.05). When analyz-
ing PTCH, the BCC patients who were TT carriers of the PTCH1 rs41313327 2350C/T gene polymorphisms had a higher expression of PTCH1 protein (median 3.31x10^5 IDV) than patients with the CT genotype (median 2.4x10^5IDV; P<.05). BCC patients carrying GG genotype in SMO rs41303402 385G/A in polymorphism had higher SMO expression than AA genotype carriers (median 3.3x10^5 IDV vs 2.9x10^5IDV, P<.05). CONCLUSION: The obtained results underline the role SHH pathway in BCC development among central European Caucasians and confirm their role as therapeutic targets for future BCC treatment regimens. CORRESPONDING AUTHOR: Aleksandra Lesiak, Department of Dermatology and Veneorology, Plac Hallera 1, 90-467 Lodz, Poland. E-mail: Lesiak_ola@interia.pl CONFLICTS: The authors have no conflicts of interest to disclose.