MauiDerm
ADVANCES IN COSMETIC + MEDICAL DERMATOLOGY

Abstracts of Poster Presentations: MauiDerm 2015

January 26–30, 2015
Maui, Hawaii

J Clin Aesthet Dermatol. 2015;8(5 Suppl 2):S1–S24

George Martin, MD
Program Director, MauiDerm; Dermatology Laser Center Maui Kihei, Hawaii

The 2015 edition of the annual MauiDerm meeting had a wide variety of clinical and scientific data presented not only at the podium, but in its poster sessions as well. A wide range of clinically relevant material was presented in poster format. For those of you who were not on hand to review the posters and discuss them with their authors, we have compiled and indexed selected posters from the 2015 meeting. It is my hope that you will find the posters informative and thought provoking.

For an alphabetical index organized by poster title or author, please see page 22 of this supplement.

ACNE

The Efficacy and Tolerability of a Fixed Combination Clindamycin (1.2%) and Benzoyl Peroxide (3.75%) Aqueous Gel in Adult Females With Facial Acne Vulgaris

Presenters: Zeichner JA

Affiliations: Zeichner JA is from Mount Sinai Medical Center, New York, New York

Objective: To investigate the efficacy and tolerability of clindamycin phosphate 1.2%/BP 3.75% gel or vehicle monotherapy in adult female acne patients.

Methods: A *post hoc* analysis in 72 adult female patients (aged ≥25 years) with moderate-to-severe acne receiving clindamycin phosphate 1.2%/BP 3.75% gel, or vehicle for 12 weeks.

Results: The efficacy of clindamycin phosphate 1.2%/BP 3.75% gel was signicantly greater than vehicle. The mean percent change from baseline in inflammatory and noninflammatory lesion counts and the percentage of patients who achieved a 2-grade reduction in the EGSS was 68.7%, 60.4% and 52.7%, respectively (P=0.019, 0.020, and 0.074 versus vehicle). In addition, 44 percent of patients reported their acne to be "clear" or "almost clear" at Week 12 (P=0.026 versus vehicle). No substantive differences were seen in cutaneous tolerability among treatment groups, and no patients discontinued treatment because of adverse events.

Limitations: It is not possible to determine the contributions of the individual active ingredients, and this study was not set up specifically to investigate the treatment of adult female acne.

Conclusions: Clindamycin phosphate 1.2%/BP 3.75% gel provides statistically significant greater efficacy than vehicle in treating adult female acne with a

favorable safety and tolerability profile.

An Aqueous Gel Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% for the Once-daily Treatment of Moderate-to-severe Acne Vulgaris: Assessment of Safety in 498 Patients

Presenters: Pariser DM, Rich P, Cook-Bolden FE, Korotzer A

Affiliations: Pariser DM is from Virginia Clinical Research, Inc., Norfolk, Virginia; Rich P is from Oregon Dermatology and Research Center, Portland, Oregon; Cook-Bolden is from Skin Specialty Dermatology, New York, New York; Korotzer A is from Valeant Pharmaceuticals, Bridgewater, New Jersey

Objective: To evaluate safety and tolerability of a fixed combination clindamycin phosphate 1.2% and benzoyl peroxide 3.75% (Clindamycin-BPO 3.75%) aqueous gel in moderate-to-severe acne vulgaris.

Methods: A total of 498 patients, 12 to 40 years of age, were randomized to receive Clindamycin-BPO 3.75% or vehicle in a double-blind, controlled, 12-week, 2-arm study evaluating safety and tolerability.

Results: No substantive differences were seen in cutaneous tolerability among treatment groups. More than 80 percent of patients treated with Clindamycin-BPO 3.75% had no erythema, >88 percent no scaling, >87 percent no itching, ≥95 percent no burning, and >95 percent no stinging at any post-baseline study visit. No patients discontinued treatment with Clindamycin-BPO 3.75% because of adverse events.

Limitations: Data from controlled studies may differ from clinical practice. It is not possible to determine the contributions from the individual active ingredients.

Conclusions: Clindamycin-BPO 3.75% provides a highly favorable safety and tolerability profile.

An Aqueous Gel Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% for the Once-daily Treatment of Moderate-to-severe Acne Vulgaris: Assessment of Efficacy in 498 Patients

Presenters: Pariser DM, Rich P, Cook-Bolden FE, Korotzer A

Affiliations: Pariser DM is from Virginia Clinical Research, Inc., Norfolk, Virginia; Rich P is from Oregon Dermatology and Research Center, Portland, Oregon; Cook-Bolden is from Skin Specialty Dermatology, New York, New York; Korotzer A is from Valeant Pharmaceuticals, Bridgewater, New Jersey

Objective: To evaluate efficacy of a fixed combination clindamycin phosphate 1.2% and benzoyl peroxide 3.75% (Clindamycin-BPO 3.75%) aqueous gel in moderate-to-severe acne vulgaris.

Methods: A total of 498 patients, 12 to 40 years of age, were randomized to receive Clindamycin-BPO 3.75% or vehicle in a double-blind, controlled, 12-week, 2-arm study evaluating efficacy (inflammatory and noninflammatory lesion counts) using Evaluator Global Severity Scores (EGSS) and subject self-assessment (SSA). In addition, patients completed a patient satisfaction survey (PSS), acne-specific QoL questionnaire, and assessed their facial skin for shininess/oiliness.

Results: Clindamycin-BPO 3.75% demonstrated statistical superiority to vehicle in reducing lesions and acne severity. Median percent change from baseline to Week 12 in inflammatory and noninflammatory lesion counts was 68.4 percent and 57.9 percent versus 35.5 percent and 32.5 percent with vehicle, respectively (both $P<0.001$). Clindamycin-BPO 3.75% showed greater efficacy relative to vehicle in assessments of skin oiliness, SSA, and PSS. Skin oiliness was reported to be none or mild by 84.7 percent of patients at Week 12 and rarely bothersome.

Limitations: Data from controlled studies may differ from clinical practice. It is not possible to determine the contributions from the individual active ingredients.

Conclusions: Clindamycin-BPO 3.75% provides statistically significant greater efficacy than vehicle in moderate-to-severe acne.

The Efficacy and Tolerability of a Fixed Combination Clindamycin (1.2%) and Benzoyl Peroxide (3.75%) Aqueous Gel in Patients With Facial Acne Vulgaris: Gender as a Clinically Relevant Outcome Variable

Presenters: Harper JC

Affiliations: Harper JC is from The Dermatology and Skin Care Center of Birmingham, Birmingham, Alabama

Objective: To investigate whether treatment differences exist in male and female patients with moderate-to-severe acne treated with clindamycin phosphate 1.2%/BP 3.75% gel or vehicle as monotherapy.

Methods: A *post hoc* analysis comparing the efficacy and cutaneous tolerability in 498 male and female patients with moderate-to-severe acne receiving clindamycin phosphate 1.2%/BP 3.75% gel, or vehicle for 12 weeks.

Results: The efficacy of clindamycin phosphate 1.2%/BP 3.75% gel was greater than vehicle ($P>0.001$) in both genders. Within the clindamycin phosphate 1.2%/BP 3.75% gel group, the mean percent change from baseline in inflammatory and noninflammatory lesion counts was greater among females than males, as was the percentage of subjects who achieved a 2-grade reduction in the EGSS ($P=0.049$).

Limitations: It is not possible to determine the contributions of the individual active ingredients.

Conclusions: Clindamycin phosphate 1.2%/BP 3.75% gel provides statistically significant greater efficacy than vehicle with a favorable safety and tolerability

profile. It appears to be more effective in female patients.

Pilot Study: Efficacy and Tolerability of a Non-Drying Topical Lotion combined with Chemical Peels in Adult Female Subjects with Moderate Facial Acne and Post-Inflammatory Lesions

Presenters: Colvan L, Goberdhan LT, Makino ET, Mehta R

Affiliations: All authors are from SkinMedica, Inc., an Allergan Company, Carlsbad, California

Background: Superficial chemical peels are often used as adjuvants to topical acne treatments as they can provide additional comedolytic effects. However combining chemical peels with these topical treatments can also result in increased side effects including dryness and irritation. Recently, a novel topical formulation (acne lotion) was developed containing high levels of antioxidants and anti-inflammatory ingredients to address sebum oxidation/peroxidation and support skin moisturization, as well as salicylic acid (2%) and 4-ethoxybenzaldehyde.

Methods: Efficacy and tolerability of a regimen including a series of three superficial chemical peels (containing lactic acid, salicylic acid, resorcinol, and retinol) and the acne lotion was evaluated in a 12-week, open-label, single-center pilot study. Eight adult female and male subjects aged 23 to 37 with moderate facial acne and Fitzpatrick skin types II to IV completed the study. Subjects received a series of three superficial chemical peels every four weeks and were instructed to apply the acne lotion twice daily (morning and evening) after cleansing. Investigator's Global Assessment of acne severity (IGA), acne lesion counts, postinflammatory hyperpigmentation or erythema (PIH/PIE), and tolerability assessments (erythema, burning/stinging, dryness/scaling and itching) were conducted at baseline and Weeks 4, 8, and 12. Standardized digital photography was taken at all visits and a self-assessment questionnaire was performed at Weeks 4, 8, and 12.

Results: The regimen provided significant reductions in mean scores for IGA at Weeks 4, 8, and 12 (all $p<0.04$). Significant reductions were also observed for PIH/PIE at all visits (all $p<0.005$). Both inflammatory and noninflammatory lesion counts consistently decreased at all follow-up visits, resulting in mean percent changes of -41.3 percent and -30.7 percent at Week 12, respectively. The chemical peel and acne lotion regimen was very well-tolerated with mean tolerability scores remaining below mild throughout the study duration. Results from the subject self-assessment questionnaire and standardized photographs support the significant improvements in efficacy observed by the investigator.

Conclusions: This pilot study suggests that the combination of new acne lotion with a series of chemical peels may provide a well-tolerated solution for adult patients seeking an effective treatment for moderate facial acne as well as post-inflammatory hyperpigmentation and/or erythema.

ACTINIC KERATOSIS

Ingenol Mebutate 0.015% Gel Follow-on Use for Multiple Actinic Keratoses on Face and Scalp: A Randomized 12-month Phase 3 Study

Presenters: Garbe C, Larsson T, Venkata R, Knudsen KM, Lear J, Seguin NB, Poulin Y

Affiliations: Garbe C is from the Department of Dermatology, Division of Dermatooncology, University Hospital Tübingen, Tübingen, Germany; Larsson T, Venkata R, and Knudsen KM are from LEO Pharma A/S, Ballerup, Denmark; Lear J is from the Department of Dermatology, Manchester Royal Infirmary and Manchester Academics Health Science Centre, Manchester University, Manchester, United Kingdom; Seguin NB is from Hopital Saint-Louis, Paris, France; Poulin Y is from Laval University, Quebec City and Center for Research in Dermatology, Quebec, Canada

Introduction: Actinic keratoses (AKs) develop in a cancerized field where epithelial cells in a photodamaged area are susceptible to the development of multiple clinically apparent and subclinical AKs, which may progress to malignancy. The chronic nature of AK necessitates repeated field treatments. Ingenol mebutate (IngMeb) gel is a novel topical field therapy for AK. We report the efficacy of IngMeb in treating AKs present after initial field treatment or those emerging in a previously cleared field.

Methods: In this Phase 3, multicenter, randomized, double-blind, vehicle-controlled study (NCT01600014), patients ≥18 years with 4 to 8 discrete AKs within a contiguous 25cm^2 treatment area on the face or scalp were treated with open-label IngMeb once daily for three consecutive days. Patients were then randomized 2:1 to IngMeb or vehicle gel if AKs were still present in the field at eight weeks after initial treatment or if AKs emerged in the previously cleared treatment field at Week 26 or 44 (emergent AKs). Patients were followed for 12 months. The primary endpoint was complete clearance of AKs in the treatment area or of those emerging in a previously cleared field eight weeks after randomization. Secondary endpoints included complete clearance in the treatment area through 12 months and change in AK lesion counts in the selected treatment area from baseline to eight weeks after randomization.

Results: The majority (87%) of patients had been previously treated for AK; median duration of AK was six years. Of 450 patients enrolled, 141 patients were randomized at eight weeks, 40 at 26 weeks, and 22 at 44 weeks after initial treatment. Overall clearance eight weeks after initial treatment was 61.6 percent; following a second treatment cycle,

IngMeb achieved a significantly greater level of clearance versus vehicle eight weeks after randomization in patients with both AKs present in the field at the initial eight-week efficacy evaluation (46.7% vs. 18.4%, respectively; p=0.001) and emergent AKs (59.5% vs. 25.0%, respectively; p=0.013). In addition, significant reductions in AK lesion counts were observed at eight weeks after randomization in patients treated with IngMeb versus vehicle, both in patients with AKs present at the initial eight-week efficacy evaluation (mean change -1.41 vs. -0.51, respectively; p<0.001) and in those with emergent AKs (-1.52 vs. -0.85, respectively; p=0.008). Of the 340 completers who were treated twice with IngMeb or once and remained clear at 8, 26, and 44 weeks, 50 percent were still clear of AKs at 12 months (95% confidence interval 44.0%, 56.1%).

Conclusions: This is the first study to investigate the efficacy of follow-up IngMeb treatment of AKs still present in the field at eight weeks after initial field treatment or of AKs emerging in a previously cleared field. At 12 months, 50 percent of patients receiving either one or two cycles of IngMeb treatment were clear of AKs. Both initial treatment with IngMeb and follow-up treatment for AKs present in the field at eight weeks and emergent AKs at 26 and 44 weeks are highly efficacious, with no decrease in efficacy after follow-up use.

Financial disclosures/funding: LEO Pharma

Survey of Patient Satisfaction with Ingenol Mebutate Gel Treatment of Actinic Keratosis from a Community Dermatology Practice

Presenters: Schaefer D

Affiliations: Schaefer D is from Austin Dermcare, Austin, Texas

Introduction: Patient-applied topical treatments for actinic keratosis (AK) are primarily used to treat areas of sun-damaged skin that contain many discrete lesions or areas of confluent AK. However, patients may be reluctant to use many of these agents because they require long durations of treatment. The duration and severity of associated local skin reactions may cause physical and visual discomfort and interfere with daily social interactions. Ingenol mebutate gel, 0.015% and 0.05%, is a topical treatment for AK that requires only a 2- to 3-day treatment regimen. The objective of this study was to report satisfaction with ingenol mebutate treatment in 26 patients from a community dermatology practice.

Methods: Dermatology patients who had received ingenol mebutate treatment of AK were invited to participate in a survey that would evaluate their response to therapy and level of satisfaction with the treatment. All participants were required to provide informed consent, have used ingenol mebutate gel, and have a clinical evaluation before and after treatment. Patients completed a questionnaire on the ease of use, tolerability, appearance of their skin after treatment, and their likelihood of repeat use of ingenol mebutate for AK. Patients were invited to provide any additional comments regarding their personal experience with the treatment.

Results: A total of 26 patients completed the questionnaire. They ranged in age from 38 to 82 years (average, 60.7 years). One patient was newly diagnosed with AK, but all of the others had a history of AK of 2 to 25 years (average, 11.6 years). A history of nonmelanoma skin cancer was reported by 19 patients (basal cell carcinoma and squamous cell carcinoma reported by 17 and 11 patients, respectively). All but two patients had received prior cryosurgery; 12 patients had used other topical therapies, most commonly fluorouracil (n=10). About half of the patients had hyperkeratotic (n=12) or recurrent (n=12) AKs. Of the 26 patients, 24 achieved 100 or ≥75-percent clearance of AKs in the area treated with ingenol mebutate. With regard to the question regarding skin appearance, respondents (n=25) indicated an excellent (n=8) or better (n=17) appearance after treatment. Patients noted that inflammation developed rapidly, but resolved after a short healing time. High satisfaction with the therapy led half of the patients to use ≥2 treatment courses of ingenol mebutate. All but one patient preferred ingenol mebutate to other AK treatments for its efficacy and the 2- to 3-day regimen. The one declining patient deemed the quantity of medication too small and not economical for the area to be treated.

Conclusions: Patients treated for AK with ingenol mebutate gel in a community dermatology practice in Austin, Texas, reported that the medicine was effective and well tolerated. They regarded the 2- or 3-day treatment regimen as more acceptable than the longer treatment courses needed with other topical therapies for AK. All respondents found the appearance of their sun-damaged skin to be excellent or better after treatment, and nearly all indicated that they would seek ingenol mebutate if future treatment was needed.

ATOPIC DERMATITIS

AN2728, A New Boron-Based Topical Anti-Inflammatory Agent, Inhibits Phosphodiesterase 4 (Pde4)

Presenters: Freund Y, Dong C, Virtucio-Frates C, Rock F, Mak Y, Zhou Y, Zane L, Jarnagin K

Affiliation: The authors are from Anacor Pharmaceuticals, Inc., Palo Alto, California.

Background: AN2728 is a boron-based topical anti-inflammatory agent currently being investigated in Phase 3 clinical trials for the treatment of mild-to-moderate atopic dermatitis.

Objective: The objectives of the studies described herein were to

further characterize the mechanism of action of AN2728.

Methods: The methodology used to characterize the mechanism of action of AN2728 included enzyme kinetic assays, phosphodiesterase-4 (PDE-4) subtype inhibition studies, protein crystallography, and an analysis of cytokine inhibition in peripheral blood mononuclear cells. In addition, to investigate reactivity against other targets, AN2728 was tested against 50 receptors and ligand-gated ion channels for inhibition at 10μM.

Results: AN2728 competes with cAMP to inhibit the PDE4B1-catalytic domain with a Ki of 173±26 nM; thus AN2728 interacts at the enzyme active site. The X-ray structure of PDE4B-catalytic domain with AN2728, and its structural relative, AN2898, reveals that the boron atom interacts with the bimetal center and occupies a position in the catalytic site similar to that of the phosphate of cAMP. AN2728 has good affinity across the PDE4 gene products, A, B, C, and D. Its selective affinity for PDE4 is 4- to 10-fold greater than its affinity for PDE1, PDE2, PDE3A, PDE6, or PDE7B. It is inactive on PDE3B, PDE5, PDE7A1, and PDE8-11. The activity of AN2728 results in an increase in intracellular cAMP and activation of PKA, followed by phosphorylation and negative regulation of transcription factors of various cytokines. In the analysis of AN2728 binding to 50 receptors and ligand-gated ion channels, inhibition was less than 25% for all of the receptors tested; thus, AN2728 is specific for PDE4.

Limitations: This study is limited by its *in vitro*, exploratory nature; future studies will further define the mechanism of action of AN2728.

Conclusions: The novel boron-containing compound, AN2728, exerts its anti-inflammatory effect by inhibition of PDE4, one of 11 subtypes of the enzymes which catalyze the breakdown of cyclic nucleotides to their inactive monophosphates (in the case of PDE4, cAMP to AMP). Through inhibition of cAMP-dependent PDE4 activity, AN2728 inhibits the production of specific cytokines with a pattern that is notably similar to that of other established PDE4 inhibitors and distinctly different from those of a glucocorticoid and a calcineurin inhibitor.

Financial disclosures/funding: This study was sponsored by Anacor Pharmaceuticals, Inc., Palo Alto, California.

BASAL CELL CARCINOMA

Randomized, Double-blind Study of Sonidegib (LDE225) in Patients with Advanced Basal Cell Carcinoma

Presenters: [1]Chang ALS, [2]Dummer R, [3]Guminski A, [4]Gutzmer R, [5]Dirix L, [6]Lewis K, [7]Combemale P, [8]Herd R, [9]Kaatz M, [10]Loquai C, [11]Stratigos A, [12]Schulze HJ, [13]Plummer R, [14]Yi T, [15]Cornélis F, [16]Kudchadkar R, [17]Trefzer U, [18]Lear J, [19]Sellami D, [20]Migden M

Affiliations: [1]Department of Dermatology; Stanford University School of Medicine, Redwood City, California; [2]Department of Dermatology, UniversitätsSpital Zürich, Skin Cancer Center University Hospital, Zürich, Switzerland; [3]Department of Medical Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; [4]Department of Dermatology and Allergy, Skin Cancer Center, Medizinische Hochschule Hannover, Hannover, Germany; [5]Department of Medical Oncology, Sint-Augustinus Ziekenhuis, Antwerp, Belgium; [6]Division of Medical Oncology, University of Colorado Cancer Center, Aurora, Colorado; [7]Oncodermatology Unit, Centre Leon Bérard, Lyon, France; [8]Consultant Dermatologist, Glasgow Royal Infirmary; Glasgow, United Kingdom; [9]Department of Dermatology and Allergology, University Hospital Jena, Freiburg, Germany and SRH Wald-Klinikum Gera GmbH, Gera, Germany; [10]Skin Cancer Center, Johannes Gutenberg-Universität Mainz, Mainz, Germany; [11]Department of Dermatology, Andreas Sygros Hospital, University of Athens, Athens, Greece; [12]Department of Dermatology, Fachklinik Hornheide, Münster, Germany; [13]Northern Centre for Cancer Care, Freeman Hospital, Newcastle Upon Tyne, United Kingdom; [14]Biometrics & Data Management, Oncology Business Unit, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [15]Cancer Center, Department of Medical Oncology, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium; [16]Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, Florida; [17]Dermatologikum Berlin, Berlin, Germany; [18]Consultant Dermatologist, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom; [19]Oncology Global Development, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [20]Departments of Dermatology and Plastic Surgery, The University of Texas MD Anderson Cancer Center, Houston, Texas

Background: The BOLT Phase 2 study, comparing two doses of sonidegib, a hedgehog pathway inhibitor (HhPI), in patients with advanced basal cell carcinoma (BCC) (aBCC; NCT01327053), met its primary endpoint of objective response rate ≥30 percent in both arms in analyses of data collected up to six months after randomization of the last patient (June 28, 2013, cutoff; median follow-up [f/u], 13.9 mo; Migden, ASCO 2014). Associations of GLI1 (marker of Hh pathway activation) with clinical outcome (as of June 28, 2013) and updated 12-month efficacy and safety data (Dec 31, 2013, cutoff; median f/u, 20.0 mo) are presented.

Methods: Patients with locally advanced BCC (LaBCC; n=194) not amenable to curative surgery or radiation or metastatic BCC (mBCC; n=36) were randomized 1:2 to receive sonidegib 200 or 800mg daily.

Clinical response was assessed by central review using modified RECIST (LaBCC) or RECIST 1.1 (mBCC). Exploratory analyses in a subset of patients (LaBCC, n=137; mBCC, n=13) assessed GLI1 levels by qRT-PCR in tumor tissue collected at baseline, Week 9, and Week 17.

Results: GLI1 levels decreased from baseline with both doses at Week 9 and 17 (median % changes [200mg], –91.07 and –93.75; $P<0.0001$ vs. baseline) and in patients with disease control (CR, PR, SD). Median percent changes (200mg) at Week 17 by response were CR, –99.47; PR, –90.79; SD, –96.58; PD, +10.19; unknown, –94.24. With an additional six-month follow-up, median exposure duration was 11.0 (200mg) and 6.6 months (800mg). More than half of patients with LaBCC in the 200mg arm responded, and tumor responses in both arms were durable. The safety profile of sonidegib was typical of HhPIs; the most common adverse events (200/800mg) were muscle spasms (52%/69%), alopecia (49%/57%), and dysgeusia (41%/60%).

Conclusions: Reduced GLI1 levels versus baseline were seen in patients with disease control. With longer follow-up, sonidegib continued to demonstrate clinically meaningful tumor shrinkage, sustained responses, and prolonged progression-free survival in patients with aBCC. The 200mg dose had a better benefit-risk profile.

Patient-reported Quality of Life (QoL) with Sonidegib (LDE225) in Advanced Basal Cell Carcinoma

Presenters: Kudchadkar R, Dummer R, Gutzmer R, Migden M, Dirix L, Lewis K, Combemale P, Higuchi K, Gogov S, Yi T, Herd R, Trefzer U, Lear J, Sellami D, Guminski A

Affiliation: [1]Department of Cutaneous Oncology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida; [2]Department of Dermatology, UniversitätsSpital Zürich, Skin Cancer Center University Hospital, Zürich, Switzerland; [3]Department of Dermatology and Allergy, Medizinische Hochschule Hannover, Hannover, Germany; [4]Departments of Dermatology and Plastic Surgery, University of Texas MD Anderson Cancer Center, Houston, Texas; [5]Department of Medical Oncology, Sint-Augustinus Ziekenhuis, Antwerp, Belgium; [6]Division of Medical Oncology, University of Colorado Cancer Center, Aurora, Colorado; [7]Oncodermatology Unit, Centre Leon Bérard, Lyon, France; [8]Worldwide Health Outcomes, Value, and Access, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [9]Oncology Clinical Development, Novartis Pharma AG, Basel, Switzerland; [10]Biometrics & Data Management, Oncology Business Unit, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [11]Consultant Dermatologist, Glasgow Royal Infirmary; Glasgow, United Kingdom; [12]Department of Dermatology, Allergology, and Tumor Therapy, Dermatologikum Berlin, Berlin, Germany; [13]Consultant Dermatologist, Manchester Royal Infirmary, Manchester, United Kingdom; [14]Oncology Global Development, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [15]Department of Medical Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia

Background: Advanced BCC can cause considerable morbidity and severe disfigurement, leading to emotional and psychological distress and reduced QoL. The hedgehog (Hh) pathway is aberrantly activated in ≥95 percent of BCCs. Sonidegib blocks the Hh pathway by selective inhibition of smoothened. In a Phase 2 study (BOLT; NCT01327053), patients with advanced BCC achieved meaningful disease control with sonidegib. The impact on patient-reported QoL is presented here.

Methods: Patients with locally advanced BCC (LaBCC) not amenable to curative surgery or radiotherapy (n=194) or metastatic BCC (mBCC; n=36) were randomized to receive sonidegib 200 or 800mg (1:2) once daily. QoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the associated Head and Neck cancer module (H&N35). Prespecified subscale scores included physical functioning, social functioning, pain, and fatigue for C30, and trouble with social contact, head and neck pain, and weight loss for H&N35.

Results: Questionnaires were completed at baseline and ≥1 baseline time point by 88.7 percent (C30) and 90 percent (H&N35) of patients. Maintenance or improvement of scores on the C30 and H&N35 scales was experienced by the majority of patients, with consistent effects in those with LaBCC and mBCC. Descriptive analysis of mean scores generally showed maintenance in each scale through Week 73 with both doses. Median time to deterioration (>10-point worsening without subsequent improvement) was 13.7 months for fatigue and 16.6 months for weight loss, and not estimable (NE) for other scales with 200mg; and 11.1, 11.3, 5.6, and 16.5 months for physical functioning, social functioning, fatigue, and weight loss, respectively, and NE for other scales with 800mg.

Conclusions: Overall, patients treated with sonidegib in the BOLT trial maintained or improved their functioning and QoL, supporting the treatment effect observed in patients with advanced BCC and the favorable tolerability of sonidegib.

HIDRADENITIS SUPPURATIVA

Safety and Efficacy of Adalimumab in Patients with Moderate to Severe Hidradenitis Suppurativa: Results from First

12 Weeks of PIONEER I, a Phase 3, Randomized, Placebo-Controlled Trial

Presenters: [1]Kimball AB, [2]Zouboulis CC, [3]Armstrong AW, [4]Korman NJ, [5]Crowley JJ, [6]Lynde C, [7]Belknap K, [7]Gu Y, [7]Williams DA

Affiliations: [1]Harvard Medical School, Boston, Massachusetts; [2]Departments of Dermatology, Venereology, Allergology and Immunology, Dessau Medical Center, Dessau, Germany; [3]University of Colorado, Denver, Colorado; [4]University Hospitals (UH) Case Medical Center, Cleveland, Ohio; [5]Bakersfield Dermatology, Bakersfield, California; [6]The Lynde Centre for Dermatology, Markham, Ontario, Canada; [7]AbbVie Inc., North Chicago, Illinois

Introduction/Objectives: This multicenter study evaluated safety and efficacy of adalimumab (ADA) in patients with moderate-to-severe hidradenitis suppurativa (HS). The 12-week, double-blind, placebo (PBO)-controlled period is reported here.

Materials/Methods: Anti-TNFα–naïve patients diagnosed with HS for ≥1 year, with total abscess and inflammatory nodule (AN) count of ≥3 and HS lesions in ≥2 body areas (Hurley Stage II or III), were randomized 1:1 to ADA (160mg at Week 0; 80mg at Week 2; 40mg weekly from Week 4) or matching PBO. Efficacy was analyzed for all randomized patients (intent-to-treat [ITT]), and safety for all ITT patients who received at least one dose of study drug. Non-responder imputation was used for missing data.

Results: The 307 ITT patients (63.8% female, 76.2% white, 20.2% black) had mean age of 37.0 years, mean HS duration of 11.5 years, and median AN count of 11. A significantly higher proportion of patients randomized to ADA achieved the primary efficacy endpoint HiSCR (Hidradenitis Suppurativa Clinical Response defined as ≥50% reduction from baseline in AN count with no increase in abscess or draining fistula counts) at Week 12; ADA (64/153, 41.8%) versus PBO (40/154, 26.0%; p=0.003). Adverse events (AE) reported by >10 percent of patients were exacerbation of HS (13.2% PBO, 9.2% ADA) and nasopharyngitis (10.5% PBO, 5.9% ADA). Cellulitis was reported by two patients for each PBO and ADA. Serious AEs included pyelonephritis (n=1 ADA) and breast cancer (n=1 PBO). No deaths occurred.

Conclusions: In PIONEER I, a Phase 3 randomized PBO-controlled study of ADA in HS, significantly more patients randomized to ADA achieved HiSCR versus patients randomized to PBO. AEs were comparable to PBO and consistent with the ADA safety profile; no new risks were identified.

ONYCHOMYCOSIS

Access of Efinaconazole Topical Solution, 10%, to the Infection Site by Spreading Through the Subungual Space

Presenters: Elewski BE, Pollak RA, Pillai R, Olin JT

Affiliations: Elewski BE is from the Department of Dermatology, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama; Pollak RA is from San Antonio Podiatry Associates, San Antonio, Texas; Pillai R is from Dow Pharmaceutical Sciences Inc., a Division of Valeant Pharmaceuticals North America, LLC., Bridgewater, New Jersey; Olin JT is from Valeant Pharmaceuticals North America, LLC., Bridgewater, New Jersey

Objective: To evaluate the ability of efinaconazole topical solution, 10% vehicle to reach the site of toenail onychomycosis by spreading through the subungual space between the nail plate and nail bed. Lacquer-based vehicles are primarily limited to application on the nail plate and dependent on nail plate permeation.

Methods: Eleven patients (mean age 48.5 years) were entered with clinically determined onychomycosis. Presence of fungal infection was confirmed by KOH testing in eight patients. Two separate applications of vehicle (with fluorescein incorporated for better visualization) were applied at the hyponychium, avoiding application to the exterior nail plate surface. Affected nails were later clipped to allow examination of the nail bed and further examination of the underside of the nail. Spread of formulation was assessed under visible and UV light conditions by photographing target toenails after vehicle application, and after nail clipping.

Results: Assessments under both visible and UV light indicated that the vehicle had spread into the subungual space, with deposition of flourescein wherever vehicle had reached, including in the nail bed. Nail clippings also indicated deposition to the underside of the nail plate.

Limitations: The relative contributions of spreading into the subungual space, or permeation through the nail plate to the efficacy of efinaconazole topical solution, 10%, in treating onychomycosis were not assessed.

Conclusions: This study suggests that the vehicle developed for efinaconazole topical solution, 10%, when applied at the hyponychium, spreads into the subungual space between the nail plate and nail bed, reaching the site of infection.

Disclosures: Drs. Elewski and Pollak were advisors to Valeant Pharmaceuticals North America, LLC. Drs Pillai and Olin are employees of Valeant Pharmaceuticals North America, LLC.

Enhancing the Transungual Delivery of Efinaconazole Through a Unique Formulation Approach

Presenters: Kircik L

Affiliations: Kircik L is from the Department of Dermatology, Indiana University School of Medicine, Indianapolis, Indiana; Physicians Skin Care, PLLC, Louisville, KY;

Department of Dermatology, Mount Sinai School of Medicine, New York, New York.

Background: Transungual delivery of an effective antifungal would seem ideal for the successful treatment of onychomycosis. However, the applied active drug must permeate through the dense keratinized nail plate and reach the deeper layers, the nail bed, and the nail matrix in sufficient concentration to eradicate the infection. So far, formulating antifungals to achieve optimal transungual delivery of active drug has been a challenge.

Methods: A unique formulation approach was employed in the development of a new topical antifungal, efinaconazole. The final alcohol-based formulation was developed from an extensive range of prototypes, and the unique combination of ingredients provides low surface tension and good wetting properties. Key properties; including keratin affinity, nail permeation, and fungicidal activity were tested in a series of *in vitro* and *in vivo* experiments.

Results: Efinaconazole was shown to have considerably lower binding to keratin, and keratin-bound drug released at a faster rate when compared to lacquer formulations like amorolfine and ciclopirox. Efinaconazole free drug and keratin release levels were at least 6-fold higher. In toenails of patients with onychomycosis, the mean concentration of efinaconazole was more than 50,000 times the MIC values (≤0.0020–0.06µg/mL) for dermatophytes recovered in Phase 3 clinical studies with efinaconazole topical solution, 10%. Efinaconazole showed comparable fungicidal activity in keratin media (mimicking the keratin-rich environment of the nail plate and nail bed) to amorolfine, and was superior to ciclopirox. In addition, efinaconazole produced a region of growth inhibition under the nail (2.52±0.42cm, mean ± SD), whereas ciclopirox 8% and amorolfine 5% nail lacquers did not.

Conclusions: The unique formulation approach to the development of efinaconazole topical solution, 10%, resulted in high concentrations of an effective, broad-spectrum antifungal in the nail bed and matrix.

Efinaconazole Topical Solution, 10%: Efficacy in Onychomycosis Patients with Co-existing Tinea Pedis

Presenters: Markinson B, Caldwell B

Affiliations: Markinson B is Chief of Podiatric Medicine and Surgery in the Leni and Peter W. May Department of Orthopedic Surgery at the Mount Sinai School of Medicine, New York, New York; Caldwell B is Assistant Dean and Professor of Clinical Education and Clinic Operations at the College of Podiatric Medicine at Kent State University, Kent, Ohio.

Objective: To evaluate efficacy of efinaconazole topical solution, 10%, in onychomycosis patients with co-existing tinea pedis.

Methods: An analysis of 1655 patients, aged 18 to 70 years, randomized to receive efinaconazole topical solution, 10%, or vehicle from two identical multicenter, double-blind, vehicle-controlled, 48-week studies evaluating safety and efficacy. The primary end point was complete cure rate (0% clinical involvement of target toenail, and both negative potassium hydroxide examination and fungal culture) at Week 52. Three groups were compared: those patients with co-existing tinea pedis on-study (treated or left untreated), and those where no co-existing tinea pedis was reported.

Results: The majorities of patients had long-standing (>5 years) onychomycosis (50.5%), more than two non-target toenails additionally affected (56.7%), and were male (77.2%). On study, 352 (21.3%) patients were reported as having co-existing tinea pedis, with 215 patients (61.1%) treated in addition to receiving efinaconazole topical solution, 10%, or vehicle for their onychomycosis. Efinaconazole topical solution, 10% was more effective than vehicle irrespective of the co-existence of tinea pedis, or its treatment. Complete cure rates of 29.4 percent were reported in those patients where co-existing tinea pedis was treated, compared to 16.1 percent where co-existing tinea pedis was not treated. Both cure rates were significant compared to vehicle, and in the latter group no patients treated with vehicle achieved complete cure.

Conclusions: Treatment of co-existing tinea pedis in onychomycosis patients enhances the efficacy of once-daily topical efinaconazole topical solution, 10%.

Onychomycosis: The Burden of Illness and Treatment Impact with Efinaconazole Topical Solution, 10%

Presenters: Tosti A, Elewski BE

Affiliations: Tosti A is from the Department of Dermatology & Cutaneous Surgery, Leonard Miller School of Medicine, University of Miami, Florida; Elewski BE is from the Department of Dermatology, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama.

Objective: To evaluate the benefits of efinaconazole topical solution, 10%, on quality of life (QoL) in onychomycosis patients.

Methods: An analysis of 1,655 patients, aged 18 to 70 years, randomized to receive efinaconazole topical solution, 10% or vehicle from two identical multicenter, double-blind, vehicle-controlled, 48-week studies evaluating safety and efficacy. The primary end point was complete cure rate (0% clinical involvement of target toenail, and both negative potassium hydroxide examination and fungal culture); clinical improvement defined as ≤10% improvement in nail involvement both at Week 52. QoL was assessed using a validated OnyCOE-t™ questionnaire. Improvement in QoL was compared in those patients clinically and not

clinically improved.

Results: Efinaconazole topical solution, 10%, was significantly more effective than vehicle irrespective of QoL domain. Greatest improvement in mean score was seen in those domains with the lowest baseline scores. All mean scores in the group considered to have clinically improved with efinaconazole exceeded 80.0 at Week 52. Mean treatment satisfaction scores with efinaconazole in those patients who were clinically improved increased from 79.9 (Week 24) to 89.2 (Week 52), compared to a corresponding drop in those patients considered not improved from 65.3 to 58.0. The correlation between change in percent affected nail and change in mean domain scores was significant with efinaconazole for all domains.

Limitations: A period of 52 weeks may be too brief to evaluate improvement in QoL in onychomycosis patients. Some of the questions in the OnyCOE-t™ questionnaire may be more relevant than others to the study population and the onychomycosis population as a whole.

Conclusions: Once-daily efinaconazole topical solution, 10%, provided statistically greater improvement in all aspects of QoL compared to vehicle. Improvement was most marked in those patients considered clinically improved and correlated with a change in percent affected nail.

Disclosures: Dr. Tosti received honorarium from Valeant as a consultant in advisory meetings. Dr. Elewski was an advisor to Valeant.

Efinaconazole Topical, 10%, for the Treatment of Toenail Onychomycosis in Patients with Diabetes

Presenters: Vlahovic TC, Joseph WS

Affiliations: Vlahovic TC is from Temple University School of Podiatric Medicine, Philadelphia, Pennsylvania; Joseph WS is from Roxborough Memorial Hospital, Philadelphia, Pennsylvania.

Objective: To evaluate efficacy, safety, and tolerability of efinaconazole topical solution, 10%, in diabetic patients with onychomycosis

Methods: A *post hoc* analysis of 112 patients, aged 29 to 70 years, randomized to receive efinaconazole topical solution, 10%, or vehicle from two identical multicenter, double-blind, vehicle-controlled, 48-week studies evaluating safety and efficacy. The primary end point was complete cure rate (0% clinical involvement of target toenail, and both negative potassium hydroxide examination and fungal culture) at Week 52.

Results: Mycologic cure rates (OC) were significantly greater with efinaconazole (56.5% and 56.3% in diabetic and non-diabetic patients, respectively) compared to vehicle (P=0.016 and P<0.001, respectively). The primary end point, complete cure, was also greater for efinaconazole (13.0% and 18.8%, respectively, vs. 3.7% and 4.7%). Treatment success (percent affected target toenail ≤10%) for efinaconazole was 40.8% and 47.7%, respectively versus 18.5% and 18.2% with vehicle. There was no statistically significant difference between the diabetic and non-diabetic populations for any efficacy endpoint. Adverse events associated with efinaconazole were local site reactions and clinically similar to vehicle.

Conclusions: Once-daily efinaconazole topical solution, 10%, may provide a useful topical option in the treatment of diabetic patients with onychomycosis.

Disclosures: Drs. Vlahovic and Joseph have served as paid consultants to Valeant. Dr. Vlahovic was a principle investigator in the pivotal trials with efinaconazole topical solution, 10%.

PSORIATIC ARTHRITIS

Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients with Psoriatic Arthritis: Pharmacodynamic Results of a Phase 3, Randomized, Controlled Trial (PALACE 1)

Presenters: Schafer PH, Chen P, Fang L, Wang A, Chopra R

Affiliations: Schafer PH and Chopra R are from Translational Development, Celgene Corporation, Summit, New Jersey; Chen P, Fang L, and Wang A are from Biostatistics, Celgene Corporation, Warren, New Jersey

Background/Purpose: Apremilast (APR) is a phosphodiesterase 4 inhibitor that helps regulate the immune response that causes inflammation and skin disease associated with psoriasis and psoriatic arthritis (PsA). PALACE 1 compared the efficacy and safety of APR with placebo in patients with active PsA despite prior conventional DMARDs and/or biologics. In this Phase 3 trial, APR demonstrated significant efficacy, including improvement in signs and symptoms and physical function related to PsA, and demonstrated maintenance of response through Week 52. This exploratory analysis evaluated the pharmacodynamic effects of APR on plasma biomarkers associated with inflammation in a subset of patients.

Methods: Patients were randomized (1:1:1) to receive placebo, APR 20mg BID (APR20), or APR 30mg BID (APR30) stratified by baseline DMARD use (yes/no). Peripheral blood plasma samples were collected from consenting patients at baseline and at Weeks 4, 16, 24, and 40 for analysis in a multiplexed cytometric bead array assay measuring 47 proteins (Human Inflammation MAP, Myriad RBM, Austin, Texas). The statistical analysis identified significant differences (P<0.05; rank ANCOVA) in the percent change from baseline among the treatment groups. Logistic regression analyses assessed the association between the percent change of the biomarkers and the achievement of an ACR20 clinical response.

Results: The biomarker subset included 150 patients (placebo: n=51; APR20: n=51; APR30: n=48).

Subjects in the biomarker subset had demographics and disease characteristics comparable with those of the full analysis set, with the exception of prior exposure to a biologic DMARD, such as a TNF blocker, which was higher in the biomarker subset (48.8%) than in the full analysis set (23.6%). In the APR20 and APR30 treatment arms, there were significantly lower percent changes from baseline, compared with placebo, for the following markers: at Week 4, interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and macrophage inflammatory protein beta (MIP-1β); at Week 16, IL-8, TNF-α, IL-6, and ferritin; and at Week 24, IL-8, TNF-α, IL-6, MIP-1β, MCP-1, and ferritin. Logistic regression analyses indicated that clinical responses correlated with the percent changes in TNF-α in the APR20 and APR30 treatment groups. A significant increase in von Willebrand Factor (vWF) was observed at Weeks 16 and 24 (although all vWF values remained within the normal range [<120µg/mL] and returned to baseline levels by Week 40). After 40 weeks of APR30 treatment, there were significant decreases in IL-17, IL-23, IL-6, and ferritin from baseline levels, and significant increases in IL-10 and IL-1 receptor antagonist from baseline levels.

Conclusions: Treatment with APR for 4 to 24 weeks was associated with significant reductions in circulating levels of IL-8, TNF-α, IL-6, MIP-1β, MCP-1, and ferritin, a range of components representing the pro-inflammatory innate M1 and Th1 immune response. After 40 weeks, there was significant inhibition of IL-6, IL-23, and IL-17 on APR30 treatment, suggesting that long-term APR therapy inhibits components of the systemic Th17 immune response, and an increase in IL-10 and IL-1RA, products of M2 macrophages. These data indicate that APR has activity against a range of immune inflammatory pathways associated with the pathogenesis of PsA.

PSORIASIS

Long-Term Safety and Efficacy of Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients With Moderate to Severe Psoriasis: Efficacy and Safety Results From a Phase III, Randomized Controlled Trial (ESTEEM 1)

Presenters: [1]Papp K, [2]Reich K, [3]Leonardi C, [4]Kircik L, [5]Chimenti S, [6]Shah K, [6]Hu C, [6]Day RM, [7]Griffiths CEM

Affiliations: [1]Probity Medical Research, Waterloo, Ontario, Canada; [2]SCIderm Research Institute and Dermatologikum Hamburg, Hamburg, Germany; [3]Saint Louis University School of Medicine, St. Louis, Missouri; [4]Physicians Skin Care, PLLC, Louisville, Kentucky; [5]University of Rome Tor Vergata, Rome, Italy; [6]Celgene Corporation, Warren, New Jersey; [7]Dermatology Centre, University of Manchester, Manchester, United Kingdom

Introduction: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to regulate inflammatory mediators.

Methods: In ESTEEM 1, patients with moderate-to-severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, body surface area [BSA] ≥10%, static Physician's Global Assessment [sPGA] ≥3) were randomized 1:2 to placebo (PBO) or APR 30mg BID (APR30). At Week 16, PBO patients were switched to APR30 through Week 32. At Week 32, patients treated with APR30 at baseline who achieved ≥75% reduction from baseline in PASI score (PASI-75) were re-randomized (1:1, blinded) to continue APR30 or receive PBO through Week 52. Upon loss of PASI-75, patients who were re-randomized to PBO resumed APR30.

Results: 844 patients were randomized (mean psoriasis duration, 19.4 years; mean PASI score, 19.0; mean BSA, 24.7%). At Week 16, significantly more patients receiving APR30 achieved PASI-75 (33.1%) versus PBO (5.3%; $P<0.0001$); primary endpoint. Mean percent change from baseline in PASI score was 52.1 percent for APR30 versus 16.7 percent for PBO ($P<0.0001$). At Week 32, 154 patients randomized to APR30 at baseline were PASI-75 responders and were re-randomized to continue APR30 (n=77) or switch to PBO (n=77). In the randomized treatment withdrawal phase, 61.0 percent of the 77 patients randomized to continue APR30 at Week 32 had PASI-75 at Week 52; 75.3 percent had ≥70% improvement in PASI score; mean percent change from baseline in PASI score at Week 52 was 80.5 percent. Of patients switched to PBO who lost PASI-75 (median time: 5.1 weeks), 70.3 percent regained PASI-75 after restarting APR30. The duration of re-treatment with APR30 through Week 52 ranged from 3.4 to 22.1 weeks.

APR was generally well-tolerated for up to 52 weeks. During the APR exposure period (defined as Weeks 0–52, including all patients who received APR, regardless of when initiated), 804 received ≥1 dose of APR30; adverse events (AEs) in ≥5 percent of patients were diarrhea (18.7%), URTI (17.8%), nausea (15.3%), nasopharyngitis (13.4%), tension headache (9.6%), and headache (6.5%). In APR-treated patients reporting diarrhea and nausea, the majority of the cases occurred within two weeks of the first dose, were predominantly mild in severity, and generally resolved within one month. The exposure-adjusted incident rate for AEs did not appear to increase over time, no new significant AEs emerged with continued exposure, and no clinically meaningful changes in laboratory measurements were reported. AEs were predominantly mild or moderate in severity. The occurrence of serious AEs was 4.2 percent and no specific serious AE was reported for >3 patients during the APR exposure period. Discontinuation rate due to AEs was low during the APR-exposure period (7.3%).

Conclusion: APR30 significantly

reduced the severity of moderate-to-severe psoriasis over 16 weeks of treatment. The clinical response for APR30 was generally maintained in patients treated for 52 weeks. APR 30 demonstrated an acceptable safety profile and was generally well-tolerated for up to 52 weeks. Most AEs were mild or moderate in severity and did not lead to discontinuation.

Psychiatric Disorders and Depression Incidence with Apremilast, an Oral Phosphodiesterase 4 Inhibitor: Pooled Analysis of the ESTEEM 1 and ESTEEM 2 Trials

Presenters: Menter A, Paul C, Day RM, Shah K

Affiliations: Menter A is from Baylor University Medical Center, Dallas, Texas; Paul C is from Toulouse University, Hôpital Larrey, Toulouse, France; Day RM and Shah K are from Celgene Corporation, Warren, New Jersey.

Introduction: Depression, suicidality, and psychiatric disturbances have been reported at higher incidences in the psoriasis population (Kurd SK. *Arch Dermatol.* 2010;146:891–895). The ESTEEM 1 and ESTEEM 2 clinical trials assessed the efficacy and safety of apremilast (APR) in patients with moderate-to-severe plaque psoriasis. The incidences of psychiatric disorders and depression were evaluated in these trials.

Methods: Patients with moderate-to-severe plaque psoriasis (PASI ≥12, BSA ≥10%, sPGA ≥3) in the ESTEEM 1 and ESTEEM 2 clinical trials were randomized (2:1) to APR 30mg BID (APR30) or placebo (PBO) through Week 16. All patients were treated with APR30 through Week 32, followed by a randomized treatment withdrawal phase through Week 52. This pooled analysis comprises data for the PBO-controlled period as well as the APR-exposure period (uncontrolled) for psychiatric events, including depression and suicidality.

Results: 1,250 patients received study medication at Week 0 (PBO: 418; APR30: 832). A total of 1,184 patients received APR30 (968 patients for ≥24 weeks and 564 for ≥52 weeks, including patients who switched from PBO to APR30 at Week 16). At screening, history of depression (13.6%) and the prior use of psychoanaleptics and psycholeptics was 11.5 and 7.1 percent, respectively. During Weeks 0 to 16, the incidence of adverse events (AEs) of psychiatric disorders was 2.9 percent in patients receiving PBO and 3.9 percent in patients receiving APR30. The incidence of AEs of depression was 0.5 percent in patients receiving PBO and 1.2 percent in patients receiving APR30. Exposure-adjusted incidence rates (EAIR) per 100 patient years were calculated as 100 × the number (n) of patients reporting the event divided by patient-years within the phase (up to the first event start date for patients reporting the event). Based on EAIR, there was no evidence of increasing incidences of psychiatric disorders (EAIR for APR30: Weeks 0 to 16, 13.9; Weeks 0 to 52, 9.1) or depression (EAIR for APR30: Weeks 0 to 16, 4.2; Weeks 0 to 52, 2.6) with longer APR treatment. Only 0.1 percent (1/1184) of patients reported serious depression; 0.1 percent (1/1184) of patients discontinued treatment because of depression during long-term APR30 exposure (Weeks 0 to 52). One patient receiving PBO committed suicide and one patient receiving APR30 attempted suicide.

Conclusions: Based on EAIR/100 patient years, there is no evidence of an increasing incidence of depression or suicidality with longer apremilast treatment. Numerical imbalances between apremilast and placebo were observed in the 16-week controlled data; however, long-term (uncontrolled) data did not reveal evidence of an increased risk of psychiatric disorders, including depression. The rate of depression reported as an adverse event was lower than the background rate in the psoriasis population (≥10%) (Hayes J. *Dermatol Ther.* 2010;23:174–180).

Effects of Apremilast on Pruritus in Patients with Moderate to Severe Plaque Psoriasis: Results From the ESTEEM 1 and 2 Trials

Presenters: [1]Papp K, [2]Yosipovitch G, [3]Bagel J, [4]Kircik L, [5]Thaçi D, [6]Lambert J, [7]Ferrandiz C, [8]Goodfield M, [9]Hu C, [9]Day RM, [10]Girolomoni G

Affiliations: [1]Probity Medical Research, Waterloo, Ontario, Canada; [2]Temple University School of Medicine, Philadelphia, Pennsylvania; [3]Psoriasis Treatment Center of Central New Jersey, East Windsor, New Jersey; [4]Physicians Skin Care, PLLC, Louisville, Kentucky; [5]University Hospital Schleswig-Holstein, Lübeck, Germany; [6]Ghent University Hospital, Gent, Belgium; [7]Hospital Germans Trias i Pujol, Barcelona, Spain; [8]Leeds General Infirmary, Leeds, United Kingdom; [9]Celgene Corporation, Warren, New Jersey; [10]University of Verona, Verona, Italy

Introduction: Psoriasis patients report itching as the most bothersome psoriasis symptom (Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. *J Am Acad Dermatol.* 2014;70:871–881.e30). Two Phase 3, randomized, controlled trials (ESTEEM 1 and ESTEEM 2) evaluated the efficacy/safety of apremilast (APR) in the treatment of moderate-to-severe plaque psoriasis. Pruritus and skin discomfort/pain results are reported up to Week 32.

Methods: Patients with moderate-to-severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, body surface area [BSA] ≥10%, static Physician Global Assessment [sPGA] ≥3) were randomized 1:2 to placebo (PBO) or APR 30mg BID (APR30). At Week 16, PBO patients were switched to APR30 through Week 32. This was followed by a randomized treatment withdrawal phase up to Week 52. Patients rated pruritus and skin discomfort on a 100mm Visual Analog Scale (VAS).

Results: The full analysis set included 844 patients from ESTEEM 1 (APR30: n=562; PBO: n=282) and 411 from ESTEEM 2 (APR30: n=274; PBO: n=137). Demographic/disease characteristics were generally well balanced between treatment groups. At Week 16, mean changes from baseline in pruritus VAS (mm) scores were significantly greater with APR30 (ESTEEM 1: -31.5; ESTEEM 2: -33.5) vs. PBO (ESTEEM 1: -7.3; ESTEEM 2: -12.2) (P<0.0001). Mean changes from baseline with APR30 represented a nearly 50-percent decrease in pruritus severity. Improvement in pruritus was observed as early as Week 2 with APR30 (P<0.001; *post hoc* analysis) and was maintained through Week 32. At Week 16, mean changes (improvements) in skin discomfort/pain VAS (mm) scores were significantly greater with APR30 (ESTEEM 1: -28.3; ESTEEM 2: -28.5) vs. PBO (ESTEEM 1: -5.0; ESTEEM 2: -9.5) (P<0.0001). At Week 16, significantly more patients achieved PASI-75 (primary endpoint) with APR30 (ESTEEM 1: 33.1%; ESTEEM 2: 28.8%) versus PBO (ESTEEM 1: 5.3%; ESTEEM 2: 5.8%) (P<0.0001). In ESTEEM, the most common AEs were diarrhea, nausea, URTI, nasopharyngitis, headache, and tension headache.

Conclusion: Improvements in pruritus were seen with APR30 as early as Week 2 and were maintained through Week 32 in patients with moderate-to-severe plaque psoriasis. The results also support the improvement of PASI score in these two studies.

Cardiovascular Risk Factors in Patients with Moderate to Severe Psoriasis: Integrated Prevalence and Safety Data from 5 Randomized Controlled Trials of Adalimumab

Presenters: Leonardi C, Gu Y, Arikan D, Lau W, Amer F

Affiliations: Leonardi C is from Central Dermatology, St. Louis, Missouri; Gu Y, Arikan D, Lau W, and Amer F are from AbbVie Inc., North Chicago, Illinois.

Introduction: Psoriasis is a systemic inflammatory disease that is associated with a high prevalence of cardiovascular (CV) comorbidity (Neimann et al. *J Am Acad Dermatol.* 2006;55[5]:829–835).

Methods: Data were integrated over 12 to 16 weeks from patients with chronic, moderate-to-severe plaque psoriasis who had been enrolled in 1 of 5 randomized placebo-controlled trials of adalimumab (ADA): M02-528 (NCT00645814), M02-538 (NCT00645905), REVEAL (NCT00237887), CHAMPION (NCT00235820), and REACH (NCT00735787). This analysis included patients with ≥1 of the following CV disease risk factors: a history of transient ischemic attack, cerebrovascular accident (CVA), angina, myocardial infarction (MI), congestive heart failure (CHF), hypertension, cardiac arrhythmia, peripheral vascular disease–arterial, congenital heart disease, coronary artery disease, diabetes, and hyperlipidemia; baseline body mass index (BMI) ≥30kg/m^2; past/current tobacco use; and age ≥65 years. We assessed the percentages of patients with ≥1, ≥2, ≥3, and ≥4 CV risk factors and the frequency of MI, CVA, and CHF in each subgroup of the population.

Results: Among 1,727 patients with psoriasis in the integrated dataset, 89.3 (n=1542), 55.0 (n=950), 26.2 (n=453), and 12.0 percent (n=207) had ≥1, ≥2, ≥3, and ≥4 risk factors, respectively. The most frequently reported risk factors were current/past tobacco use (65.6%), baseline BMI ≥30kg/m^2 (48.0%), hypertension (28.4%), hyperlipidemia (22.4%), and diabetes (9.4%). The numbers and types of risk factors were balanced between the ADA and PBO groups.

When grouped by ≥1, ≥2, ≥3, and ≥4 risk factors, percentages of patients in the ADA versus PBO group experiencing an event were: MI (1.2% vs. 1.5%, 2.0% vs. 2.4%, 3.5% vs. 4.1%, and 8.1% vs. 8.3%); CVA (0.4% vs. 0.6%, 0.7% vs. 0.9%, 1.4% vs. 1.8%, and 3.3% vs. 3.6%) and CHF (0% vs. 0.2%, 0% vs. 0.3%, 0% vs. 0.6%, and 0% vs. 1.2%), respectively.

Conclusion: This integrated analysis of the data from five randomized controlled trials of ADA in patients with moderate-to-severe psoriasis found that underlying CV risk factors were common in the clinical trials, exceeding the elevated prevalence of CV risk factors observed in a practice-based psoriasis population (Neimann 2006). The incidences of CV events (MI, CVA, and CHF) in patients with psoriasis with ≥1 to ≥4 CV risk factors in the ADA arm were slightly lower than those in the placebo arm, regardless of the number of risk factors.

Financial disclosures/funding: Dr. Leonardi has served as a consultant for AbbVie, Amgen, Dermira, Janssen, Boehringer-Ingelheim, Eli Lilly, Leo, Sandoz, UCB, and Pfizer; has served as an investigator for AbbVie, Amgen, Anacor, Celgene, Coherus, Eli Lilly, Galderma, Janssen, Merck, Pfizer, Stiefel, Leo, Novartis, and Tolmar; and is part of the speakers' bureau for AbbVie. Drs. Gu, Arikan, Lau, and Amer are employees of AbbVie and may hold AbbVie stock or stock options. The authors and AbbVie scientists designed the study and analyzed and interpreted the data. All authors contributed to the development of the content; all authors and AbbVie reviewed and approved the abstract; the authors maintained control over the final content. Medical writing support was provided by Jennifer Han, MS, of Complete Publication Solutions, LLC, Horsham, PA. AbbVie funded the research and medical writing support.

Five-Year Interim Results from the ESPRIT 10-year Postmarketing Surveillance Registry of Adalimumab for Moderate to severe Psoriasis

Presenters: Thaçi D, Kerdel F,

Bereswill M, Williams DA

Affiliations: Thaçi D is from Comprehensive Center for Inflammation Medicine, University Medical School Schleswig Holstein, Campus Lübeck, Germany; Kerdel F is from Florida Academic Dermatology Centers, Miami, Florida; Bereswill M is from AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany; Williams DA is from AbbVie Inc.North Chicago, Illinois

Introduction: ESPRIT, a 10-year international observational registry, is prospectively evaluating long-term effectiveness and safety of adalimumab (ADA) in adults treated for moderate-to-severe chronic plaque psoriasis (NCT00799877). This is an interim analysis of safety and effectiveness over a five-year period from September 26, 2008 through November 30, 2013.

Methods: ESPRIT enrolled patients continuing ADA treatment from a current prescription or previous study participation, or initiating ADA within four weeks of entering the registry (New-Rx Population). The All-Rx Population received ≥1 ADA dose in this registry. Patients are evaluated at three and six months, then every six months for up to 10 years. As-observed effectiveness parameters include Physician's Global Assessment (PGA) and quality of life (DLQI; US only). Incidence rates (IR) are reported for observational adverse events (AEs) as events per 100 patient years of observation (E/100PY). A standardized mortality ratio (SMR; ratio of observed to expected treatment-emergent deaths) of <1.0 indicates that the observed mortality rate was below expected in an age-, sex-, country-matched population.

Results: The All-Rx population (N=6059) included 2,580 (42.6%) New-Rx pts. Median registry exposure was 765 (range 14–1892) days for All-Rx and 677 days for New-Rx. 10.6 percent of All-Rx and 13.1 percent of New-Rx patients discontinued the registry, most frequently from loss to follow-up (3.6% and 4.5%, respectively). Among All-Rx patients: 57.6 percent were male; median age and weight at baseline were 47 (range 18–94) years and 87 (range 41–252) kg. The IRs of serious AEs and AEs leading to death were 5.5 E/100PY and 0.3 E/100PY. SMR was 0.30 [95% CI: 0.19, 0.44]. IR of serious infection was 1.2 E/100PY, including disseminated TB in two patients; two opportunistic infections were reported. The overall IR for malignancies was 1.1 E/100PY; IR for nonmelanoma skin cancer was 0.6 E/100PY; IR for melanoma was <0.1 E/100PY. 55.0, 57.0, 58.3, 60.1, 63.5, and 64.7 percent of All-Rx pts achieved PGA "clear" or "minimal" at 6, 12, 24, 36, 48, and 60 months of treatment in the registry, respectively.

Conclusion: No new safety signals were observed with ADA treatment. IR of serious infection and malignancies remained stable compared to the four-year interim report (Kerdel, et al. *J Eur Acad Dermatol Venereol.* 2013;27(s4):68. Abs P174). The observed number of deaths was below that expected. As-observed effectiveness remained stable through 60 months. This research was funded by AbbVie Inc.

Financial disclosures/funding: The authors and AbbVie scientists designed the study, and analyzed and interpreted the data. AbbVie funded the research and provided writing support. All authors contributed to the development of the content; all authors and AbbVie reviewed and approved the presentation; the authors maintained control over the final content. Thaçi D received honoraria from AbbVie, Amgen, Biogen-Idec, Celgene, Janssen, Leo, Novartis, and Pfizer for participation on ad boards and as a speaker, and from AbbVie and Leo for consultancy; and received research grants from AbbVie, Leo, and Pfizer. Kerdel F received honoraria from AbbVie, Amgen, Celgene, Janssen, Leo, Pfizer, and Stiefel for participation as a speaker; and received grants from AbbVie, Amgen, AstraZeneca, Celgene, Janssen, and Pfizer, for participation as an investigator. M Bereswill and D Williams receive a salary as employees of AbbVie and may also receive AbbVie stock, stock options, and/or stock grants. The authors would like to acknowledge Jody Bennett, employee of AbbVie, for medical writing support in the production of this abstract.

Results After at Least 52 Weeks of Open Label Treatment with Ixekizumab, an Anti-IL-17A Monoclonal Antibody, in a Phase 2 Study in Chronic Plaque Psoriasis

Presenters: Gordon KB, Leonardi C, Lebwohl M, Cameron G, Erickson J, Braun D, Banerjee S, Heffernan M

Affiliations: Gordon KB is from the Department of Dermatology, Northwestern University, Feinberg School of Medicine, Chicago, Illinois; Leonardi C is from Saint Louis University School of Medicine, St. Louis, Missouri; Lebwohl M is from Mount Sinai School of Medicine, New York, New York; Cameron G, Erickson J, Braun D, and Banerjee S are from Eli Lilly and Company, Indianapolis, Indiana

Background: Ixekizumab, an anti-IL-17A monoclonal antibody, has been shown to be effective in patients with moderate-to-severe chronic plaque psoriasis following 20 weeks of randomized, placebo-controlled therapy in a Phase 2 study. The efficacy and safety of ixekizumab after at least 52 weeks of additional treatment in an open-label extension (OLE) were evaluated.

Materials/Methods: During the Randomized Treatment Period (RTP), patients received ixekizumab (10, 25, 75, or 150mg) or placebo subcutaneously at 0, 2, 4, 8, 12, and 16 weeks. At Week 20, patients entered a treatment-free period (Weeks 20 to 32) and were eligible to enter an OLE at Week 32 or at the time when response to treatment fell below a PASI 75. Patients who entered the OLE were treated with

120mg ixekizumab subcutaneously every four weeks. Efficacy was evaluated after 52 weeks in the OLE, and safety was evaluated over at least 52 weeks of treatment in the OLE.

Results: Of the 129 patients who completed the RTP, 120 entered the OLE, and 103 (86%) completed at least 52 weeks of OLE treatment. Overall, a PASI 75, PASI 90, or PASI 100 response was observed in 90, 79, or 57 percent of patients, respectively, and an sPGA (0) or sPGA (0,1) was achieved in 58 and 77 percent, respectively, following 52 weeks of OLE treatment. The mean percent improvement in PASI from the baseline of the RTP was 91 percent after 52 weeks in the OLE. Among patients initially assigned to placebo (n=22), 95 percent (18/19) showed a PASI 75 response, 95 percent (18/19) a PASI 90 response, and 63 percent (12/19) a PASI 100 response after 52 weeks of OLE treatment. Overall, 67 percent of patients had a treatment-emergent adverse event in the OLE, the most common being nasopharyngitis (10%), upper respiratory tract infection (8%), sinusitis (4%), and diarrhea (4%), and eight percent had a serious adverse event. There were no deaths and no cases of tuberculosis or invasive fungal infections.

Conclusions: In patients previously treated with ixekizumab in the RTP, response to treatment was maintained in a significant majority of patients following 52 weeks of OLE therapy. In addition, patients who received placebo in the RTP responded to ixekizumab treatment at rates similar to those seen in patients treated with ixekizumab in the RTP. Safety signals observed over at least 52 weeks of observation were consistent with previously reported results in the RTP in this patient population.

Secukinumab Shows Sustained Response in Subjects with Moderate-to-severe Plaque Psoriasis: A Subanalysis of the ERASURE Phase 3 Study

Presenters: Lebwohl M, Vender R, Menter A, Papavassilis C

Affiliations: Lebwohl M is from Mount Sinai Hospital, New York, New York; Vender R is from McMaster University, Hamilton, Ontario, Canada; Menter A is from Baylor University Medical Center, Dallas, Texas; Papavassilis C is from Novartis Pharma AG, Basel, Switzerland.

Introduction: Secukinumab (AIN457), a fully human anti-interleukin-17A monoclonal antibody demonstrated superior efficacy when compared with placebo at Week 12 in the ERASURE Phase 3 clinical study. In addition, it also showed long-term efficacy with an acceptable safety profile at Week 52 in subjects with moderate-to-severe plaque psoriasis. This subanalysis further evaluates sustainability of response to secukinumab to Week 52.

Methods: In this 52-week, multicenter, double-blind, placebo-controlled study (NCT01365455), subjects aged ≥18 years were randomized (1:1:1) to subcutaneous secukinumab 300mg (n=245), 150mg (n=245), or placebo (n=248) once weekly at Baseline, Weeks 1, 2, and 3, and then every four weeks from Week 4 to 48. For this subanalysis of data to Week 52, summary statistics by treatment group were tabulated for percentage of subjects who sustained a ≥75, ≥90, and 100-percent improvement from Baseline in Psoriasis Area and Severity Index score (PASI 75, PASI 90 and PASI 100) or a score of 0/1 on a modified 5-point investigator's global assessment (IGA mod 2011 0/1). A sensitivity analysis was performed with multiple imputations.

Results: The primary endpoint of PASI 75 and IGA mod 2011 0/1 responses at Week 12 with secukinumab 300mg and 150mg versus placebo were met in this study ($P<0.001$ for each dose vs. placebo). Clinical response rates further improved to Week 16, with percentage of PASI 75, PASI 90, PASI 100, and IGA mod 2011 0/1 responders being, respectively, 91.7, 73.6, 43.0, and 78.7 percent in the secukinumab 300mg group and 81.6, 56.2, 22.7, and 62.2 percent in the secukinumab 150mg group. At Week 52, PASI 75, PASI 90, PASI 100, and IGA mod 2011 0/1 responses were sustained, respectively, in 83.5, 65.4, 41.8, and 67.3 percent of subjects in the secukinumab 300mg group and 70.1, 42.2, 23.7, and 50.2 percent in the secukinumab 150mg group. For all PASI 75 and IGA mod 2011 0/1 responses, numerically higher response rates were seen with the secukinumab 300mg dose as compared with the 150mg dose through Week 52. Secukinumab was well-tolerated with no unexpected safety findings.

Conclusion: These results showed a sustained high response to secukinumab in subjects with moderate-to-severe plaque psoriasis over 52 weeks, with 300mg exhibiting greater sustainability than the 150mg dose.

Financial disclosures/funding: This research was funded by Novartis Pharma AG. These results were previously presented at the 23rd EADV Congress, October 8–12, 2014, Amsterdam, The Netherlands.

Patient Perspectives in the Management of Psoriasis: US Results From the Population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) Survey

Presenters: Lebwohl MG, Armstrong AW, Van Voorhees AS, Kalb RE, Kavanaugh A

Affiliations: Lebwohl MG is from The Icahn School of Medicine at Mount Sinai, New York, New York; Armstrong AW is from the Department of Dermatology, University of Colorado at Denver, Aurora, Colorado; Van Voorhees AS is from the Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania; Kalb RE is from the Department of Dermatology, State University of

New York at Buffalo School of Medicine and Biomedical Sciences Medical Group, Buffalo, New York; Kavanaugh A is from the University of California at San Diego, La Jolla, California.

Introduction: To gain further insight into real-world treatment trends and unmet needs from the patient and physician perspectives, the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) survey of 3,426 patients and 781 physicians in North America and Europe was conducted. We report results from the subset of US patients participating in the survey.

Methods: Telephone numbers for this household survey were randomly selected by list-assisted random digit dialing. Adults diagnosed with psoriasis and/or psoriatic arthritis (PsA) participated. Patients did not have to be currently under the care of a healthcare provider (HCP), a patient organization member, or receiving treatment.

Results: From 52,926 US households screened, 1,005 adults completed the survey. The US household prevalence of psoriasis was 4.0 percent; the extrapolated population prevalence was 2.2 percent. A diagnosis of psoriasis alone was reported by 73.1 percent of patients; 26.9 percent indicated a diagnosis of PsA (± a separate diagnosis of psoriasis). Severe disease was reported by 29.5 percent of patients with psoriasis and 55.9 percent with PsA. The most important factors contributing to symptom severity in psoriasis patients were itching (36.1%) and location or size of skin lesions (21.8%). In PsA patients, the most important factors were pain or swelling of joints (48.1%) and itching (14.8%). Although most patients had seen an HCP in the past 12 months, ≈20 percent of patients who had not seen an HCP reported it was because they did not think their HCP could help. About 23 percent of psoriasis patients and 55 percent of PsA patients reported ever having a discussion with their current HCP about conventional oral or biologic therapies. Current or prior conventional oral therapy was reported by 14.8 percent of psoriasis and 52.2 percent of PsA patients; 30.3 percent (psoriasis) and 46.1 percent (PsA) of these patients were taking these medications at the time of the survey, whereas the majority had discontinued therapy. Only 8.6 percent of psoriasis patients reported ever having used biologic therapy versus 42.6 percent of PsA patients; ≈60 percent of these patients were receiving biologics at the time of the survey, whereas the rest had discontinued. At the time of the survey, 21.6 percent of patients reported no current treatment; 9.3 percent of psoriasis and 50.0 percent of PsA patients were receiving systemic therapy. Perceived treatment burden, safety/tolerability concerns, and lack of effectiveness were associated with treatment dissatisfaction and discontinuation.

Conclusion: Psoriasis and PsA remain undertreated in the United States, marked by high treatment dissatisfaction and discontinuation. Several unmet needs are identified and warrant further attention.

Tofacitinib or Etanercept versus Placebo on Patient-reported Outcomes: Results from a Phase 3 Study in Moderate to Severe Chronic Plaque Psoriasis

Presenters: Valenzuela F, Lahfa M, Tan H, Papacharalambous J, Mamolo C

Affiliations: Valenzuela F is from the University of Chile Clinical Hospital, Department of Dermatology, Santiago, Chile; Lahfa M is from the Hôpital Larrey, Toulouse, France; Tan H, Papacharalambous J, and Mamolo C are from Pfizer Inc, Global Innovative Pharmaceuticals, Groton, Connecticut

Introduction/Objectives: Tofacitinib is an oral Janus kinase inhibitor being investigated for the treatment of psoriasis. In this Phase 3, double-blind, 12-week, placebo-controlled study (OPT Compare: NCT01241591), tofacitinib 5mg and 10mg twice daily (BID) were efficacious in patients with chronic plaque psoriasis as measured by Psoriasis Area and Severity Index (PASI) and Physician's Global Assessment (PGA); tofacitinib 10mg BID was non-inferior to etanercept 50mg twice weekly (BIW). Here we evaluated the effect of both doses of tofacitinib or etanercept vs placebo on patient-reported outcomes (PROs).

Materials/Methods: 1,101 adult patients received tofacitinib 5mg BID (n=329), tofacitinib 10mg BID (n=330), etanercept 50mg subcutaneously BIW (n=335), or placebo (n=107). PRO endpoints: change from baseline in the Dermatology Life Quality Index (DLQI) score, Itch Severity Item (ISI) score, and Short Form-36 (SF-36) physical and mental component summary (PCS and MCS) scores; the proportion of patients reporting a Patient's Global Assessment (PtGA) response of "clear" or "almost clear"; and the proportion of patients "very satisfied" or "somewhat satisfied" with their study medication.

Results: A substantial disease burden in the study population was evident by mean scores at baseline across multiple PROs (DLQI: 12.3-13.3; ISI: 5.2-5.3; PCS: 46.8–48.3; MCS: 39.8–42.0). At Week 12, mean changes from baseline in DLQI were -7.3, -9.7, -9.0, and -1.9 for tofacitinib 5mg BID, tofacitinib 10mg BID, etanercept 50mg BIW and placebo, respectively (p<0.0001 for all vs. placebo). Mean changes in other PROs were: -3.2, -4.0, -3.5, and -0.4 for ISI; 4.1, 5.0, 5.2, and 0.8 for PCS; and 5.0, 7.6, 5.8, and 1.5 for MCS, for tofacitinib 5mg BID, tofacitinib 10mg BID, etanercept 50mg BIW and placebo, respectively (p<0.0001 for all vs. placebo). The proportion of PtGA responders was 32.7, 56.3, 53.1, and 1.1 percent for tofacitinib 5mg BID, tofacitinib 10mg BID, etanercept 50mg BIW and placebo groups, respectively (p<0.0001 for all vs.

placebo). The majority of patients reported being "somewhat satisfied" or "very satisfied" with treatment at Week 12: 71.0, 85.9, and 86.0 percent in the tofacitinib 5mg BID, tofacitinib 10mg BID, and etanercept 50mg BIW groups, respectively, versus 31.6 percent for placebo ($p<0.0001$ for all). Tofacitinib was generally efficacious and well-tolerated. The most frequent adverse events were nasopharyngitis and upper respiratory tract infections.

Conclusions: Both doses of tofacitinib significantly improved multiple aspects of quality of life as measured by several PROs; this reflected improvements in efficacy. PRO results with tofacitinib 10mg BID were comparable to those with etanercept 50mg BIW, suggesting that oral tofacitinib may represent an important new treatment option for moderate-to-severe psoriasis.

Psoriasis Patients With PASI 90 Response Achieve Greater Health-related Quality of Life Improvements than Those With PASI 75 to 89 Response

Presenters: McLeod L, Mallya UG, Fox T, Zhao Y, Mordin M, Strober B

Affiliations: McLeod L is from RTI Health Solutions, Research Triangle Park, North Carolina; Mallya UG and Zhao Y are from Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; Fox T is from Novartis Pharma AG, Basel, Switzerland; Mordin M is from RTI Health Solutions, Ann Arbor, Michigan; Strober B is from University of Connecticut Health Center, Farmington, Connecticut and Probity Medical Research, Waterloo, Ontario, Canada

Introduction/Objectives: Secukinumab (AIN457), a fully human anti-interleukin 17A monoclonal antibody, was evaluated in Phase 3 clinical studies for efficacy and safety in subjects with moderate-to-severe plaque psoriasis. Previous reports showed evidence for secukinumab's efficacy with respect to Psoriasis Area and Severity Index (PASI) 75 and 90 response at Week 12 and to Investigator's Global Assessment (IGA) mod 2011 response (0 or 1) at Week 12. This analysis evaluates the further benefit on patient-reported outcome (PRO) responses of achieving improvements in objective skin clearing (as defined by PASI 90 status vs. PASI 75–89 status).

Materials/Methods: ERASURE and FIXTURE, two multicenter Phase 3 trials, were used in this pooled analysis. Patients aged ≥18 years were randomized 1:1:1 in ERASURE to subcutaneous treatment groups (secukinumab 150mg, secukinumab 300mg, and placebo) and 1:1:1:1 in FIXTURE (including an etanercept 50mg twice-weekly group). PROs were assessed using the Dermatology Life Quality Index (DLQI) and the visual analog scale (VAS) from the EuroQoL 5-Dimension Health Status Questionnaire (EQ-5D) at baseline and Weeks 4, 8, 12, 24, 36, and 52. Subjects achieving clinical response (PASI 90 or PASI 75-89) and PRO meaningful response (DLQI [0 or1] or EQ-5D VAS (>7 points) were compared using the chi-square test.

Results: Among the 1,144 subjects randomized to secukinumab (150mg, n=572; 300mg, n=572), 550 (48.3%) were PASI 90 responders, and 292 (25.5%) were PASI 75 to 89 responders at Week 12. Subjects achieving both clinical response and DLQI response were significantly higher among the PASI 90 compared with PASI 75 to 89 responders at Week 12 (70.0% vs. 48.1%; $P<0.05$). The response rates were similar between PASI 90 and PASI 75 to 89 responders (73.8% vs. 70.9%; $P>0.05$) who achieved EQ-5D VAS response at Week 12.

Conclusions: Psoriasis skin clearing is related to improvements in some measures of health-related quality of life and health status, with a meaningful reduction in DLQI associated with better improvements in objective skin clearing (PASI 90 vs. PASI 75–89).

URTICARIA

Safety of Omalizumab in Patients with Chronic Idiopathic/ Spontaneous Urticaria (CIU/CSU): Pooled Analysis of Three Randomized, Double-blind, Placebo-controlled Phase III Studies (ASTERIA I, ASTERIA II, and GLACIAL)

Presenters: Casale T, Saini SS, Kaplan A, Maurer M, Rosén K, Aydin S

Affiliations: Casale T is from the University of South Florida, Tampa, Florida; Saini SS is from Johns Hopkins Asthma and Allergy Center, Baltimore, Maryland; Kaplan A is from The Medical University of South Carolina, Charleston, South Carolina; Maurer M is from the Department of Dermatology and Allergy Charité–Universitätsmedizin, Berlin, Germany; Rosén K is from Genentech Inc., South San Francisco, California; Aydin S is from Novartis Pharma AG, Basel, Switzerland.

Introduction/Objectives: The safety profile of omalizumab, a humanized anti-IgE monoclonal antibody, for the treatment of moderate-to-severe allergic asthma is well-established. Omalizumab is the first and only approved (Europe and US) therapy for the treatment of chronic idiopathic/spontaneous urticaria (CIU/CSU) in adult and adolescent (≥12 years) patients with inadequate response to H1-antihistamines. Here we report the pooled safety data from three Phase III studies.

Materials/Methods: The safety and tolerability of omalizumab in 975 CIU/CSU patients were investigated in the ASTERIA I, ASTERIA II, and GLACIAL Phase III studies. Patients in ASTERIA I and ASTERIA II were symptomatic despite approved doses of H1-antihistamines and were randomized to receive omalizumab 75mg, 150mg, or 300mg, or placebo. Patients in GLACIAL received omalizumab 300mg or placebo and were symptomatic despite H1-antihistamines (up to 4X approved dose) plus H2-antihistamines,

leukotriene-receptor antagonists or both. Safety was evaluated at Week 12 (treatment period for ASTERIA II and a pre-specified timepoint in ASTERIA I and GLACIAL), and Week 24 (treatment period for ASTERIA I and GLACIAL).

Results: The overall incidence of adverse events (AEs:≥1) was similar across studies between patients receiving omalizumab 75mg (68.5%), 150mg (74.9%), 300mg (77.7%) versus placebo (68.6%). The majority of treatment-related AEs were mild or moderate in severity across treatment groups. Incidence of AEs of special interest, such as injection site reactions and arterial thrombotic events were low and similar across studies for omalizumab versus placebo. Frequency of AEs reported to be caused by omalizumab was similar with placebo for 12- or 24-week treatment periods. No additional AEs of special interest were identified in the studies. The overall incidence of serious AEs (SAEs) was similar between patients receiving omalizumab 75mg (2.1%), 150mg (3.4%), 300mg (6.1%) versus placebo (5.0%). No SAEs were suspected to be caused by omalizumab, and no patients withdrew from treatment due to omalizumab-related SAEs. No anaphylactic reactions, malignancies or deaths related to omalizumab were observed during the studies. No patient developed anti-omalizumab antibodies.

Conclusions: No new safety signals were identified compared with the established safety profile of omalizumab for the treatment of moderate-to-severe allergic asthma. Safety data were similar for all omalizumab-treated groups and placebo for both 12- and 24-week treatment periods. Safety data to-date support omalizumab as a well-tolerated treatment option for patients with CIU/CSU.

Financial disclosures/funding: This study was funded by Novartis and Genentech, Inc. Clinicaltrials.gov ID: NCT01287117, NCT01292473, NCT01264939

Correlation Between Changes in Urticaria Symptoms and Sleep Experience in Patients with Chronic Spontaneous/Idiopathic Urticaria (CSU/CIU): Results from Two Randomized, Double-blind, Placebo-controlled Phase III Trials of Omalizumab

Presenters: Stull D, Mcbride D, Houghton K, Balp M

Affiliations: Stull D, Mcbride D, and Houghton K are from RTI Health Solutions, Health Economics, Didsbury, United Kingdom; Balp M is from Novartis Pharma AG, Basel, Switzerland.

Introduction/Objectives: Patients with chronic spontaneous/idiopathic urticaria (CSU/CIU) report negative effects on sleep (e.g., interference with sleep and sleep disruption), which have consequences, such as tiredness, daytime somnolence, and lack of energy. As there is no information on the association between improvement in urticaria signs and symptoms and improvements in sleep or reductions in daytime somnolence, the current study explores the correlations between the trajectories of change shown in the Weekly Urticaria Activity Score (UAS7) and Medical Outcomes Study (MOS) Sleep Scale (daytime somnolence and sleep disturbance subscales) across 40 weeks.

Material/Methods: Data were obtained from two Phase III trials (ASTERIA I and GLACIAL), investigating the efficacy of omalizumab in patients with refractory CSU/CIU. Patient-reported outcome (PRO) data were collected at baseline and Weeks 4, 12, 24, and 40. Urticaria signs (wheals) and symptoms (itching) were measured using the UAS7. Effects on sleep were measured using two domains of the MOS Sleep Scale (a 12-item PRO comprising six theoretical dimensions that measure key aspects of sleep): daytime somnolence and sleep disturbance. Data were analyzed using latent growth modelling (LGM) wherein individual slopes of change and intercepts for UAS7 and MOS daytime somnolence and sleep disturbance were correlated for each patient.

Results: In both trials, mean baseline UAS7 score was 30 out of 42, mean MOS somnolence score was 40 out of 100, and mean sleep disturbance score was 47 out of 100. These scores decreased to 10 for UAS7, 25 for MOS somnolence, and 29 for sleep disturbance at Week 24. LGM analysis found that changes in UAS7 and MOS daytime somnolence were correlated at 0.67 (ASTERIA I) and 0.72 (GLACIAL) indicating moderate-to-strong correspondence between changes in signs and symptoms and daytime somnolence. This positive correlation indicates that the knowledge of a patient's signs and symptoms of urticaria provides good insight into the extent of daytime somnolence. Changes in the UAS7 and MOS sleep disturbance subscale were correlated at 0.53 (ASTERIA I) and 0.59 (GLACIAL). A patient's UAS7 score yields moderate insight into their sleep disturbance and vice-versa.

Conclusions: These results indicate strong empirical evidence that sleep is negatively affected by urticarial signs and symptoms. Further, these results appear to be the first to use data from all assessment points simultaneously to demonstrate that improvements in urticaria result in substantial reductions in daytime sleepiness and sleep disruption.

Financial disclosures/funding: This study was funded by Novartis and Genentech, Inc. Clinicaltrials.gov ID: NCT01287117, NCT01264939.

Alphabetical Index

BY ARTICLE TITLE

BY AUTHOR