PA-01: A Phase 2, Multicenter, Double-Blind, Randomized, Vehicle Controlled Clinical Study to Assess the Synergistic Effect of a Halobetasol/Tazarotene Fixed Combination in the Treatment of Plaque Psoriasis

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DISCLOSURES: LHK is an advisor and investigator for Ortho Dermatologics and Dow Pharmaceutical Sciences. TL and RP are employees of Bausch Health.

BACKGROUND: Fixed combinations are commonplace in dermatology, providing significant efficacy and tolerability benefits. In some cases, two active ingredients complement each other providing a cumulative or additive effect. In rarer cases, a synergistic effect may be seen where the sum of the two active ingredients’ combined action is greater than the sum of the efficacy of the constituent parts. Being able to demonstrate synergy is important in situations where the two active ingredients may be used individually to provide layering.

OBJECTIVE: To determine whether a novel halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) fixed combination lotion provides a synergistic effect in the treatment of moderate-to-severe plaque psoriasis.

METHODS: Post hoc analysis of 212 patients with moderate-to-severe plaque psoriasis randomized (2:2:2:1) to HP/TAZ lotion, HP, TAZ, or vehicle once-daily for 8 weeks, with a 4-week post-treatment follow-up. Treatment success was evaluated based on two outcomes: percent of patients achieving at least a 2-grade improvement in Investigator Global Assessment (IGA) and IGA score equating to “clear” or “almost clear”; and percent change from baseline in the IGA multiplied by Body Surface Area (BSA) composite score, a simple validated alternative to assessing response to therapy that correlates well with the Psoriasis Area Severity Index (PASI). Synergy was calculated by summing up the contribution of the individual active ingredients (HP and TAZ) to overall efficacy and comparing to the efficacy achieved with HP/TAZ lotion relative to vehicle.

RESULTS: At Week 8, treatment success with HP/TAZ lotion, relative to vehicle, was 42.8% compared with 23.6% and 9.0% for HP and TAZ. Percent change from baseline in IGAxBSA score, relative to vehicle, was 51.6% compared with 37.3% and 3.3% for HP and TAZ. In both cases the synergy ratios were 1.3. At Week 12, treatment success with HP/TAZ lotion, relative to vehicle, was 31.3% compared with 14.1% and 5.9% for HP and TAZ. Percent change from baseline in IGAxBSA score, relative to vehicle, was 47.3% compared with 25.7% and 8.6% for HP and TAZ. Synergy ratios were 1.6 and 1.4, respectively.

LIMITATIONS: This was a post hoc analysis in moderate-to-severe psoriasis.

CONCLUSIONS: Halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) fixed combination lotion provides a synergistic effect in the treatment of moderate-to-severe plaque psoriasis. In addition, by combining two agents into one once-daily formulation, this novel formulation reduces the number of product applications and may help patient adherence.

PA-02: A Phase 2, Multicenter, Double-Blind, Randomized, Vehicle-Controlled Clinical Study to Compare the Safety and Efficacy of a Halobetasol Propionate 0.01% Lotion and Halobetasol Propionate 0.05% Cream in the Treatment of Plaque Psoriasis

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DISCLOSURES: FAK, ZDD, and SKT are advisors to Ortho Dermatologics and investigators with Dow Pharmaceutical Sciences. TL and RP are employees of Bausch Health.

BACKGROUND: Potent topical corticosteroids (TCS) are commonly used to treat plaque psoriasis. Halobetasol...
propionate 0.05%, as a cream or lotion, has been shown to be highly effective in treating psoriasis short-term. Advances in formulation development may provide lower concentrations of TCS to be used, without compromising efficacy and affording longer-term use.

OBJECTIVE: To investigate the efficacy and safety of a once-daily application of a novel halobetasol propionate 0.01% lotion (HP lotion) in comparison with halobetasol propionate 0.05% cream (HP cream, Ultravate®) in patients with moderate-to-severe plaque psoriasis.

METHODS: Multicenter, randomized, double-blind, vehicle-controlled Phase 2 study in moderate or severe psoriasis (N=150). Patients randomized (2:2:1 ratio) to receive HP 0.01% lotion, HP 0.05% cream, or vehicle once-daily for 2 weeks. Efficacy assessments included treatment success (defined as at least a 2-grade improvement from baseline in the Investigator Global Assessment [IGA] and a score of “clear” or “almost clear”), impact on individual signs of psoriasis (erythema, plaque elevation, and scaling) at the target lesion, and improvement in Body Surface Area (BSA). Safety and treatment emergent adverse events (TEAEs) were evaluated throughout.

RESULTS: HP 0.01% lotion and HP 0.05% cream were statistically equivalent at 2 weeks for all efficacy assessments; whereby 30.0% and 31.6% of patients were treatment successes, respectively (P=0.854). At Week 2, 2-grade improvements in erythema, plaque elevation, and scaling were achieved in 38.3%, 40.0%, and 43.3% of patients, respectively, compared with 31.6% (P=0.446), 36.8% (P=0.727), and 47.4% (P=0.663) with HP 0.05% cream. BSA was improved by 22.3% compared with 20.9% with HP 0.05% cream (P=0.787). There were two treatment-related application-site reactions (one each in the HP 0.01% lotion and vehicle groups), both were mild-to-moderate. There were no reports of skin atrophy, striae, telangiectasia, or folliculitis.

LIMITATIONS: This was a 2-week label restricted study.

CONCLUSIONS: Halobetasol propionate 0.01% lotion was comparable to the higher concentration halobetasol propionate 0.05% cream in achieving treatment success, reducing psoriasis signs of erythema, plaque elevation, and scaling at the target lesion, and improving BSA following 2 weeks daily-treatment. Both treatments were well-tolerated over the short duration of the study.

PA-03: Achievement of the National Psoriasis Foundation Treatment Targets Among Patients in Ixekizumab Clinical Trials: Analysis of Pooled Uncover Results

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BACKGROUND/OBJECTIVE: National Psoriasis Foundation (NPF) published treatment targets for US patients with plaque psoriasis. We retrospectively analyzed the data from UNCOVER-1, -2, and -3 studies using these treatment target goals.

METHODS: Data were integrated from the 12-week induction period of Phase 3 studies (UNCOVER-1, -2, & -3), wherein subjects received 80-mg ixekizumab every 2 weeks (IXEQ2W; US-labelled dose; N=1169) after a 160-mg starting dose. Data for etanercept (ETN) treatment per label (50-mg biweekly; N=740) and placebo (PBO; N=792) through Week 12 were analyzed and presented. At Week 12, 82% of IXEQ2W-treated subjects achieved Static Physician’s Global Assessment (sPGA) 0.1 and were re-randomized (UNCOVER-1 and -2 only), and the results for the US-labelled dosing of Q2W–Q4W are presented. Treatment response was evaluated based on NPF treatment target consensus; acceptable response as body surface area (BSA) ≤3% or BSA improvement ≥75% at 12 weeks of treatment, and targeted response as BSA ≤1% at 12 weeks and every 6 months thereafter. All response rates between treatment groups were compared using Cochran-Mantel-Haenszel test stratified by study. Missing data were imputed as nonresponse.

RESULTS: At 12 weeks, 74% of subjects achieved acceptable response with IXE and 36% with ETN. The targeted response was achieved in 52% of IXE-treated subjects and 15% of ETN-treated subjects. 89% of subjects achieved the targeted response at 6 months (Week 36) and 87% at 12 months (Week 60) post-induction. All comparisons to IXEQ2W were statistically significant (p<.001) using CMH test. *ETN was included in 2 of the 3 UNCOVER studies. Only subjects with sPGA (0,1) values at 12 weeks in the Induction Phase entered the Maintenance Phase, and were divided into 3 treatment arms; this was 82% of the subjects who were initially randomized.

CONCLUSION: IXE-treated subjects per US-labelled dosing achieved and maintained a high level of skin clearance, according to the NPF treatment targets.

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PA-04: Air Pollution, Autophagy, and Skin Aging: Impact of Particulate Matter 10 (PM10) on Human Dermal Fibroblasts

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BACKGROUND: World Health Organization report from 2016 states that more than 3 million people die annually from air pollution, which places air pollution as the world’s largest single environmental health risk factor. Particulate
matter (PM) is one of the main components of air pollution, and there is increasing evidence that PM exposure exerts negative effects on the human skin.

**OBJECTIVES:** To see the impact of air pollution on skin aging, we analyzed the effect of PM exposure on human dermal fibroblasts (HDFs) with Western blot, enzyme-linked immunosorbent assay, and gene analysis.

**METHODS:** Cultured HDFs were exposed to PM10 at a concentration of 30 mg/cm² for 24 h, and their gene/protein expression of inflammatory cytokines, fibroblast chemical mediators, and autophagy were assessed.

**RESULTS:** A total of 1977 genes were found to be differentially expressed following PM exposure. We observed a significantly increased expression of pro-inflammatory genes. Protein expression of IL-6 and IL-8 also significantly increased. In addition, there was a significant increase in CYP1A1, CYP1B1, MMP-1, and MMP-3 mRNA expression, while a significant decrease in TGF-b, COL1A1, COL1A2, and elastin mRNA expression in PM-exposed dermal fibroblasts. Protein expression of MMP-1 was significantly increased and that of TGF-b and procollagen profoundly decreased, similar to the gene analysis results. Autophagy, an integrated cellular stress response, was also increased while transmission electron microscopy analysis provided evidence of PM internalization in the autolysosomes.

**CONCLUSION:** Taken together, our results demonstrate that PM10 contributes to skin inflammation and skin aging via impaired collagen synthesis. Increased autophagy in our study suggests a reparative role of autophagy in HDFs stressed with PM, but its biological significance requires further research. Further findings will be discussed.

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**PA-05:** An Open-Label Study of the Safety of HP40, a 40% (w/w) Hydrogen Peroxide Topical Solution, in Patients with Seborrheic Keratoses

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**INTRODUCTION:** Seborrheic keratosis (SK) is one of the most common benign skin lesions, affecting more than 80 million Americans. HP40 is a 40% (w/w) hydrogen peroxide topical solution approved for the treatment of SK. Efficacy and safety of HP40 in patients with SK have been demonstrated in two pivotal studies. We sought to assess the safety of HP40 after up to 4 treatments of SK target lesions on the trunk, extremities, or face.

**METHODS:** This open-label safety study (NCT02667288) enrolled patients aged ≥18 years with 4 eligible SKs. Eligible lesions were stable, typical SKs, with both length and width measuring 5 to 15 mm and with ≤2 mm thickness, and were located on the trunk, extremities, or face. HP40 was applied to all 4 target lesions by the investigator or designee on Day 1. During subsequent treatment visits at 3-week intervals (Days 22, 43, and 64), only SKs with a Physician’s Lesion Assessment (PLA) score >0 were retreated (PLA: 0=clear; 1=near clear; 2=thickness ≤1 mm; 3=thickness >1 mm). Patients were followed for 84 days after the fourth treatment visit (total 148 days). Safety was assessed at all visits, including end of study (Day 148).

**RESULTS:** The study enrolled 147 patients (588 lesions total) with mean age of 68.4 years and Fitzpatrick types I to VI (80% were Types II and III). Treatment-emergent AEs (TEAEs) were reported for 25 (17%) patients, and all were reported mild or moderate in intensity. The most frequently reported TEAEs were cough, seasonal allergy, and sinusitis (2% each). No serious AEs were reported; no patient discontinued due to AEs. Local skin reactions (LSRs) were predominantly mild and most commonly included transient pruritus, stinging, crusting, edema, erythema, and scaling that usually resolved by next visit. The majority of lesions had no LSR by Day 148, and the few reported LSRs were generally mild: There were no reports of atrophy, edema, erosion, ulceration, or vesicles; and no reports of erythema, hypopigmentation, or scarring in 92%, 93%, and 99% of lesions, respectively.

**CONCLUSION:** Four treatment sessions of HP40 topical solution 40% were safe and well tolerated for the treatment of patients with seborrheic keratosis.

**DISCLOSURES:** Valerie D. Callender, Ellen H. Frankel, Jonathan S. Weiss, and William P. Werschler are investigators for Aclaris Therapeutics, Inc. Christopher Powala and Stuart D. Shanler are employees of Aclaris Therapeutics, Inc., and may own stock/stock options in that company. Brian B. Beger and Esther Estes are former employees of Aclaris Therapeutics, Inc.

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**PA-06:** An Update on the Long-Term Safety Experience of Ixekizumab: Results from the Psoriasis Clinical Development Program with More Than 3 Years of Follow-Up from 12 Clinical Trials and More Than 15,000 Patient-Years of Exposure to Ixekizumab

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**BACKGROUND:** In moderate-to-severe plaque psoriasis (psoriasis), maintaining adequate control of disease activity
generally requires long-term treatment. Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin (IL)-17A, and has shown substantial clinical effect in patients with psoriasis, with a short-term safety profile consistent with and comparable to that of high-dose etanercept (UNCOVER-2 and -3). We recently presented our long-term update on >12,000 patient-years (PY) revealing a consistent safety profile over time.

**OBJECTIVE:** Here we summarize integrated safety data based on 15212.5 patient-years of IXE exposure during 12 clinical trials in patients with psoriasis.

**METHODS:** Treatment-emergent adverse event (TEAE) data were integrated from 12 IXE clinical trials (controlled and uncontrolled) in psoriasis, including three pivotal phase 3, randomized, controlled, double-blind clinical trials (UNCOVER-1, -2, and -3). Exposure-adjusted incidence rates (IRs) for TEAES within 12-week time periods through 168 weeks (>3 years) of treatment were summarized. IR was expressed as the number of unique events for a given category of TEAE per 100 PY, based on the entire duration of exposure during each 12-week period. Major Adverse Cerebro-cardiovascular Events (MACE) were assessed by an external adjudication committee.

**RESULTS:** The total for all patients exposed to IXE (N=5871) was 15,212.5 PY of exposure (median, 1142 days; maximum, 2236 days). In this population, 4640 patients were treated with IXE for at least 1 year, 3201 patients were treated for at least 2 years, and 2981 patients were treated for at least 3 years. Overall TEAEs occurred with an IR (95% CI) of 228.0 (220.0, 236.3) per 100 PY during the first 12 weeks’ exposure to IXE and decreased or remained similar in subsequent 12-week intervals, with an IR of 118.1 (110.2, 126.6) during the period from Week 156 to Week 168. The IRs (per 100 PY) for the TEAES of infections, injection-site reactions, allergic reactions/hypersensitivities, and malignancies during Weeks 0 to 12 decreased or remained similar in subsequent 12-week intervals up to Week 156 to Week 168. The most commonly reported events were infections of the upper respiratory tract (viral or unspecified), which were generally mild or moderate in severity. Most injection-site reactions events were mild or moderate in severity. The IR (all treatment periods) for adverse events leading to treatment discontinuation was 2.8 (2.6, 3.1) per 100 PY. The IR for serious adverse events was 5.6 (5.2, 6.0) per 100 PY. The IR for deaths per 100 PY was 0.2; while the IRs for safety topics of special interest were as follows: serious infections (1.3); oral candidiasis (0.9); MACE (0.5); non-melanoma skin cancer (NMSC, 0.3); malignancies excluding NMSC (0.5); and inflammatory bowel disease (0.2).

**CONCLUSIONS:** The safety profile of long-term Ixekizumab treatment with up to 3 years of continuous use remains consistent with previous report, with no evidence of cumulative toxicity.

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**PA-07:** ARDS and Septic Shock Secondary to Leflunomide Induced Pustular Psoriasis

We present a 63-year-old female from a Burmese refugee camp with a past medical history significant for rheumatoid arthritis (RA), type 2 diabetes mellitus, hypertension, hyperlipidemia, presenting with right foot itching, pain, and diffuse body rash.

The patient had had three admissions prior to this with the same rash that started out as small pruritic maculopapular eruptions. The current episode started a month ago with a right foot, rash starting on her medial-posterior calf and progressively extending. There was no history of cuts, bites, stings, trauma, new medications, recent travels, fever, or chills. She had no complaints of chest pain, shortness of breath, palpitations, headache, dizziness, loss of consciousness, blurry vision, extremity weakness, abdominal pain, abnormal bowel or bladder habits, change in sleep, appetite, or weight. She used a cane at baseline but her walking had recently been affected with the right leg pain.

She was being followed by Rheumatology for many years and managed for severe rheumatoid arthritis. During the past 7 years, she had undergone different treatment regimens including colchicine, nonsteroidal, steroids, methotrexate, and leflunomide. Her best control was found to be on leflunomide, which had been started around a year ago. Unfortunately, she started getting these rashes, which had been addressed by her primary care physician and rheumatologist at various times as cellulitis and cutaneous RA and treated with antibiotics in addition to the leflunomide she had been receiving. Blood work at various times in the past had shown positive rheumatoid factor, ESR, CRP; but negative antinuclear antibody, CCP antibody. She had an Immuno Globulin Release Assay (IGRA) negative for tuberculosis workup.

Over the hospital course, the patient rapidly deteriorated. She developed respiratory failure, necessitating progressively higher supplemental oxygen, was intubated for ARDS, and also developed septic shock from a ventilator associated pneumonia. Dermatology and Rheumatology were consulted for management. Dermatology were of the opinion that the lesions could be pustular psoriasis and recommended prompt treatment with cyclosporine and acetrin in addition to avoiding further insults with steroids or disease-modifying antirheumatic drugs. She was on multipronged treatment with broad spectrum antibiotics as well as the combination of cyclosporine and acetrin. During the prolonged ICU stay, skin biopsies were obtained and revealed “aggregates of neutrophils between degenerated and flattened keratinocytes within the upper layer of the epidermis along with psoriatic changes,” which was typical for pustular psoriasis. She gradually started improving, was weaned off...
of vasopressors, successfully exubated, and her rashes began to slowly fade as well. Her care team correlated her pustular psoriasis with the use of leflunomide given the chronology of disease presentation and the improvement off of the offending agent, and she was started on infliximab instead. She was discharged under stable condition and is currently following up with Dermatology and Rheumatology as outpatient without further recurrences.

**PA-08: Assessing Patient Concerns Regarding Seborrheic Keratoses on the Face: Comparison Against Other Cosmetic Concerns**

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**INTRODUCTION:** There has been continued growth in the demand for noninvasive aesthetic treatments. While seborrheic keratoses (SKs) represent one of the most common benign skin lesions in humans that frequently appear on highly visible areas such as the face and hairline, relatively little is known about patient concerns related to SKs within the context of other common aesthetic concerns.

**METHODS:** An online survey of US consumers was conducted from September 28 to October 13, 2017. Eligible survey participants were aged 35 to 65 years and were previously diagnosed with SKs by a healthcare provider or self-confirmed the presence of SKs using the definition and example images provided for the survey. Eligible participants must have been bothered by appearance of SKs located on the face or hairline (score ≥3 on a 5-point Likert scale [1=not at all bothered; 2=slightly bothered; 3=somewhat bothered; 4=moderately bothered; 5=extremely bothered]).

Participants answered questions related to perceptions of their SKs and their concerns about SKs in relation to other common aesthetic concerns.

**RESULTS:** The total of 702 adults completed the survey (mean age, 50 years; female, 80%). Of these, 10% were aged 35 to 39 years, 40% each were aged 40 to 49 years or 50 to 59 years, and 10% were aged 60 to 65 years. The mean household income was $120,566. Respondents were non-Hispanic white/Euro-American (62%), East Asian/Asian American (13%), Hispanic/Latin American (12%), African American (10%), multi-ethnic/racial (3%), and South Asian/Indian American (1%). A total of 62% of survey participants reported being extremely bothered or very bothered with the appearance of SKs located in highly visible areas, including the face and hairline (mean Likert scale score, 3.8). When asked to rank in order their three key aesthetic concerns (ie., which issue they would address first, second, and third), participants most commonly selected excess body fat (23%), facial/hairline SKs (19%), and facial lines/wrinkles (13%) ahead of unwanted hair on face or body (9%), uneven skin tone (8%), and sagging facial skin (8%). Facial/hairline SKs were more commonly chosen as a top-three concern (45%) ahead of unwanted hair on face or body (31%), uneven skin tone (31%), sagging facial skin (26%), or submental fat (24%). Survey participants also responded that the treatments they were extremely interested or very interested in were noninvasive skin rejuvenation procedures such as chemical peels and microdermabrasion (48%), dental aesthetics (43%), hair removal (40%), injectable fillers (26%), and neurotoxin injections (25%). When presented with a top-three product to treat facial/hairline SKs, 597 participants (85%) found the product to be extremely appealing or very appealing.

**CONCLUSION:** Highly visible SKs on the face and hairline are of significant aesthetic concern to survey participants, and comparable to excess body fat and facial wrinkles. A majority of survey participants demonstrated a strong interest in noninvasive treatment modalities for SK lesions.

**DISCLOSURES:** Shuai Xu, MD, MSc, reports consulting for Aclaris Therapeutics. He also reports grant support from Pfizer Inc, Leo Pharma, and Novartis. Stacy Wang, PharmD, is an employee of Aclaris Therapeutics, Inc.

**PA-09: Assessing Patient Satisfaction with Hydrogen Peroxide Topical Solution, 40% (w/w) Treatment of Seborrheic Keratoses on the Face, Neck, and Décolletage: Objectives and Design of the Phase 4, Open-Label SK-FAN Study**

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**ABSTRACT:** Seborrheic keratoses (SKs) are benign cutaneous lesions affecting ~84 million individuals in the US. A proprietary hydrogen peroxide topical solution 40% (w/w) (HP40) is approved by the US Food and Drug Administration for the treatment of raised SKs. This report describes the methodology of a Phase 4, open-label study designed to assess participants’ satisfaction following HP40 treatment of SKs located on the face, neck, and décolletage. Eligible participants were aged 30 to 75 years with a diagnosis of stable, clinically typical SKs, including 2 target SKs located on the face and 1 target SK located on the neck or décolletage. Target SKs had Physician Lesion Assessment™ (PLA) of ≥2 on a 4-point scale (0=clear; 1=near clear; 2=thin [≤1 mm]; 3=thick [>1 mm]), were 5 to 15 mm in diameter, and were treated with HP40 on study day 1, and days 15 and 29 if lesions met criteria for treatment. Patient satisfaction was assessed predose (day 1), 24 hours after the day 2 dose, 1 week after day 15 and 29 dosing, and on days 85 and 113 (study end) using the...
Subject Satisfaction Assessment (SSA; 1=not satisfied at all; 2=slightly satisfied; 3=moderately satisfied; 4=satisfied; 5=very satisfied). The primary outcome measure was Question #4 of the SSA, “On a scale of 1–5, rate your level of satisfaction with the appearance of your skin treated with [HP40].” The secondary outcome measure was Question #3 of the SSA, “On a scale of 1–5, rate your level of satisfaction of your treatment experience.” Question #10 and its 4 constructs of confidence, attractiveness, embarrassment, and comfort with being photographed were tertiary outcome measures. Exploratory outcome measures were predose and postdose SSA ratings. Additional analyses were correlations between PLA and SSA scores, and predictors of treatment satisfaction (ie, participant characteristics). A total of 30 participants were enrolled at 3 US centers. Data analyses are currently ongoing with results expected in early 2019.

DISCLOSURES: Janet DuBois has been a principal investigator for and received payment from Accutis, Aclaris Therapeutics, Alexar Therapeutics, Allergan, Atacama Therapeutics, Athenex, Botanix, Braintree Laboratories, Brickell Biotech, Cellectix, Cutanea Life Sciences, Dermata Therapeutics, Dermavant Sciences, Dermira, DFB Soria, DUSA, Endo International, Escalier Biosciences, Foamix, Gage Development Company, Galderma USA, GlaxoSmithKline, Glenmark Generics, Incyte, Kiniksa, LEO Laboratories, Medimetriks, Moberg, Mylan, Naked Biome, Nielsen Bioscience, Novan, Novartis, Perring, Pfizer, Promius, Santalis, Seeghpharm, Siena Biopharmaceuticals, Sol-Gel, Taro, Teva, Tolmar, and Valeant. Kimberly Grande is an investigator for Aclaris Therapeutics and has received grants for clinical studies, and has received honoringa as a speaker for Aclaris. Judith Schnyder and Stuart D. Shanler are employees of Aclaris and may own stock/stock options in that company.

PA-10: Assessing the Safety and Efficacy of Fixed-Dose Combination Calcipotriol 50 µg/g Plus Betamethasone 0.5 mg/g (as Dipropionate) Gel in Adolescent Patients with Psoriasis

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BACKGROUND/OBJECTIVES: Psoriasis is a chronic, recurrent, immune-mediated inflammatory disorder that commonly manifests in adolescence. Around 30 to 50% of adults with psoriasis develop the disease before the age of 20; 25% are diagnosed between 10 and 19 years of age. Topical formulations containing corticosteroids and/or vitamin D3 analogues are recommended for treating psoriasis. The US Food and Drug Administration (FDA) has approved fixed-dose combination calcipotriol 50 µg/g plus betamethasone 0.5 mg/g (as dipropionate) (Cal/BD) gel for treating body and scalp psoriasis in adults, and scalp psoriasis in adolescents. This Phase 2 study, part of a post-approval commitment to the FDA, evaluated Cal/BD gel in adolescents with psoriasis on body and scalp.

MATERIALS/METHODS: This was a prospective, multicentre, non-controlled safety study in patients aged 12 to <17 years with body (trunk and/or limbs) and scalp psoriasis. All patients had at least mild psoriasis according to the 5-point physician’s global assessment of disease severity (PGA), which affected ≥3% body surface area and ≥10% scalp area. Cal/BD gel was applied once daily for up to 8 weeks, with study visits at baseline and weeks 2, 4, 6, and 8. Patients with clear skin at week 4 discontinued the study, while those with clear skin at weeks 2 and 6 discontinued treatment but remained in the study. The primary objective was to evaluate the safety of Cal/BD gel, primarily based on the incidence of adverse drug reactions (ADRs) and adverse events (AEs). Efficacy was a secondary objective, assessed based on the proportion of patients with controlled disease (defined as “clear” or “almost clear” skin [PGA of 0/1]), the percentage surface area of body and scalp affected by psoriasis, and patient assessments of itch on the body and itch-related sleep loss (assessed by a visual analogue scale, 0–100 mm), among others.

RESULTS: In total, 107 patients (median age 14 years; range 12–16) were enrolled and treated with Cal/BD gel; 14 (13.1%), 87 (81.3%), and 6 (5.6%) had mild, moderate, and severe disease by PGA (body), respectively. Eight ADRs were observed in 8 patients; decreased blood cortisol was the only ADR reported in 1 patient (n=1). Overall, 59 (55.1%) patients experienced at least one AE; the most common were headache and nasopharyngitis (n=6, 5.6% for both). At week 4 and at end of treatment (last observation carried forward), 43.3% (n=45/104) and 57.9% (n=62/107) of patients had controlled disease (body). Mean (±SD) body and scalp surface area affected by psoriasis decreased from 14.9±8.3% at baseline to 7.7±8.5% and 4.4±7.8% at weeks 4 and 8, respectively. Patients’ assessment of itch (mean 28.4±24.9, 8.5±16.1, and 7.3±15.1) and sleep loss (mean 10.5±18.6, 6.8±15.3, and 5.6±14.0) decreased from baseline to week 4 and end of treatment, respectively.

CONCLUSIONS: This study demonstrates that Cal/BD gel is well tolerated and effective for treating scalp and body psoriasis in adolescents.

PA-11: Cardiovascular Risk in Patients with Behçet’s Disease: A Nationwide Population-Based Dynamic Cohort Study

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BACKGROUND: Behçet’s disease (BD) is a chronic inflammatory multisystem disease of unknown etiology. The risk of cardiovascular disease (CVD) in BD is not well understood. Several studies have previously investigated thromboembolitis and thrombosis in both arteries or veins in BD patients. However, there are few studies that address the correlation between Behçet’s disease (BD) and cardiovascular risk.

OBJECTIVE: Identification of an association with CVD and BD would both improve our understanding of the pathogenesis of BD and help to identify an appropriate diagnostic workup for cardiovascular risk in affected patients. Therefore, we investigated the cardiovascular risk in patients with BD using a nationwide insurance database in Korea. This study aims to determine the overall cardiovascular risk in BD patients compared to that in controls.

METHODS: Patients with BD (n =5,576) with no previous history of cardiovascular diseases were selected from the Korean National Health Insurance Database (from 2010 to 2014). An age- and sex-matched control population of individuals without BD (n=27,880) was randomly sampled at a ratio of 5:1. Both cohorts were followed for incident cardiovascular disease or until 2015.

RESULTS: The risks of myocardial infarction (hazard ratio [HR]=1.717 [1.08-2.73]) and stroke (HR=1.653 [1.094-2.498]) were significantly higher in BD patients than they were in control patients. BD patients also had a significantly higher risk of all cause death (HR=1.823 [1.4-2.373]) compared to the controls.

LIMITATIONS: This study has several limitations. The first limitation is that we did not obtain data regarding potential cardiovascular-associated covariates, including smoking habits, alcohol consumption, body mass index, and family history. In addition, the disease severity and the drugs used to treat BD, which may influence the risk of cardiovascular disease, were unclear. Third, the cause of death was not confirmed. Therefore, further studies regarding the relationship of BD and CVD are needed to substantiate our findings.

CONCLUSION: This study evaluated the cardiovascular risk in Korean patients with BD compared to age- and sex-matched controls. We found that patients with BD had a higher incidence in MI, stroke, and all cause death than did those without BD. Patients with BD, therefore, must be carefully screened for cardiovascular risk. Further studies are needed to clarify the relationship between BD and cardiovascular diseases.

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DISCLOSURES: KC16E1S0917

CONFLICTS OF INTEREST: None declared.

FUNDING: This study was supported by grants from the National Research Foundation of Korea (No. NRF-2016R1C1B1008288), funded by the Korean Ministry of Science, ICT, and Future Planning (MSIP).

PA-12: Clinical Efficacy of a Novel Two-Part Skincare System on Pollution-Induced Skin Damage

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ABSTRACT: Air pollution remains to be a global health concern, and recent studies have shown that air pollutants can accelerate skin aging and skin damage through several pathways that induce oxidative stress, skin barrier dysfunction, apoptosis, and inflammation.

Preventive measures need to be considered to maintain optimal skin health, and topical skincare products may be able to reverse the negative effects of air pollution on skin.

A randomized, double-blind, placebo-controlled clinical usage study was conducted to assess the efficacy and tolerability of a novel two-part skincare system (LVS) that was developed to provide protection against environmental skin aggressors including air pollution. This system, which consisted of a DAY product and a NIGHT product, was assessed on pollution-induced skin damage and compared to placebo when used for 8 weeks. The placebo-controlled clinical study was performed between October and December 2017 in New Delhi, India, which had an average Air Quality Index (AQI) greater than 300 (considered as “Hazardous”) for the duration of the study, and subjects were required to live and/or work in a severely polluted urban environment. Study endpoints included clinical efficacy assessments, standardized digital photography, subject self-assessment questionnaires, sebum samples, and skin biopsy samples.

After 8 weeks of use in subjects exposed to extremely high levels of pollution, LVS provided significant improvements compared to placebo in all clinical grading efficacy parameters including crow’s feet wrinkles, overall skin damage, skin tone evenness, tactile roughness, and visible redness. Subject self-assessment questionnaires showed that the treatment product was highly rated in self-perceived efficacy. Histological analyses of biopsy samples using biomarkers related to skin structure, damage and function (collagen IV, MMP1, CPD, and CD1a) further support the clinical benefits of LVS. Decreased SQOOH and MDA content in skin swab samples suggest that LVS helped to reduce oxidative stress in patients’ skin.

The presented study is among the first to show that topical skincare products can help to reduce pollution-induced skin damage and enhance skin quality, especially when specifically formulated with active ingredients that
combat the harmful effects of air pollutants. The results show that LVS is able to reduce pollution-induced oxidative stress resulting in clinically improved skin quality.

**PA-13: Clinical Signs of Epithelial Surface Disruption Impact Pain and Sexual Health in Patients with Moderate-to-Severe Genital Psoriasis**

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**BACKGROUND:** In genital psoriasis, cutaneous and mucosal lesions of the genital area can present with erosions, fissures, and ulcers, clinical signs of epithelial surface disruption.

**OBJECTIVE:** This post-hoc subset analysis evaluated the impact of these signs on pain and sexual activity in patients with moderate-to-severe genital psoriasis and the effect of ixekizumab (IXE) treatment in this subgroup of patients.

**METHODS:** Patients with moderate-to-severe genital psoriasis from a double-blind, randomised, placebo-controlled phase 3 study, receiving either placebo or IXE 160 mg at week 0, followed by IXE 80 mg every 2 weeks (IXEQ2W), were analyzed for presence of genital erosions, fissures, and/or ulcers at baseline through week 12. In this analysis, these signs were correlated with patient-reported outcomes (PROs) on pain and sexual activity using generalized linear models and the effect of treatment on primary and secondary outcome measures in this subgroup was analyzed.

**RESULTS:** At baseline, 38% (n=57) of patients presented with genital erosions, fissures, and/or ulcers. This subset had significantly higher scores in the Genital Psoriasis Symptom Scale (GPSS) total (p=0.018), the GPSS Pain (p=0.013), and the GPSS Discomfort (p=0.043), with significantly higher mean and summary scores for genital pain, stinging, and burning (p=0.025) compared to patients without fissures/erosions/ulcers. This subgroup also differed significantly in the static Physician General Assessment of Genitalia (sPGA-G) score (p=0.002). The differences in GPSS total and GPSS for pain, stinging, and burning between the subgroups with and without epithelial surface disruption were also significant when analyzing the subpopulation with an overall body surface area (BSA) involvement <10%. Evaluation of how often genital psoriasis limited frequency of sexual activity at baseline confirmed that patients without fissures/erosions/ulcers were more likely to not be limited sexually by their disease (odds ratio [OR] 4.17 vs 3.33) with an overall 25% greater OR over the 12 week observation period. Improvement of genital erosions, fissures, and/or ulcers in response to treatment with IXEQ2W was paralleled by reduced severity in pain and sexual health-related PROs.

**CONCLUSION:** These data emphasize the distinct phenotype of genital psoriasis that can present with erosions, fissures, and/or ulcers, clinical features that contribute to disease severity and impact genital pain and sexual health in patients with moderate-to-severe genital psoriasis even in the absence of higher BSA involvement. Treatment with IXEQ2W improved genital psoriasis severity, genital pain, and sexual health.

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**FUNDING:** This study was funded by Eli Lilly and Company Limited.

**PA-14: Conjunctivitis Adverse Events in Dupilumab Clinical Trials**

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**BACKGROUND:** Dupilumab (anti-IL-4Rα mAb) inhibits its signaling of IL-4/IL-13, key drivers of Type 2 allergic diseases such as atopic dermatitis (AD), asthma, chronic rhinosinusitis with nasal polyposis (CRSwNP), and eosinophilic esophagitis (EoE). Dupilumab is approved for the treatment of adults with uncontrolled moderate-to-severe AD.

**OBJECTIVES:** We reviewed incidence, severity, and resolution of conjunctivitis in patients from dupilumab clinical trials in AD, asthma, CRSwNP, and EoE.

**METHODS:** “Conjunctivitis” comprised all MedDRA Preferred Terms containing conjunctivitis. Randomized, double-blind, placebo-controlled dupilumab trials were: (1) primary safety pool (R668-AD-1021, LIBERTY AD SOLO 1/SOLO 2): adults with moderate-to-severe AD; (2) LIBERTY AD SOLO-CONTINUE: dupilumab-treated patients from SOLO1&2 who achieved Investigators’ Global Assessment score of 0/1 [clear/almost clear] or 75% improvement from baseline in Eczema Area and Severity Index at Week (WK) 16 in SOLO 1/2; (3) LIBERTY AD CHRONOS: adults with moderate-to-severe AD; (4) LIBERTY AD CAFÉ: adults with AD and inadequate response to/intolerance of/medically inadvisable for cyclosporin A; (5) DRIII2544: adults with uncontrolled persistent asthma; (6) LIBERTY ASTHMA QUEST: adults/adolescents with uncontrolled moderate-to-severe asthma; (7) LIBERTY ASTHMA VENTURE: adults/adolescents with glucocorticoid-dependent severe asthma; (8) ACT12340: adults with CRSwNP refractory to intranasal corticosteroids; and (9) R668-EE-1324: adults with active EoE.
RESULTS: Conjunctivitis incidence was higher in dupilumab-treated vs placebo patients in all AD trials except SOLO-CONTINUE. Conjunctivitis rates, as % patients with ≥1 event (hazard ratio 95% CI), were: primary safety pool: WK16 q2w/qw/combined 9.3% (4.43[2.30–8.51])/7.9% (3.80[1.95–7.40])/8.6% (4.13[2.21–7.72]), vs placebo 2.1%; CHRONOS: WK52 q2w+concomitant topical corticosteroids [TCS]/qw+TCS/combined 13.6% (1.76[0.93–3.33])/19.4% (2.51[1.57–3.99])/17.9% (2.31[1.47–3.63]), vs placebo+TCS 7.9%; CAFÉ: WK16 q2w+TCS/qw+TCS/combined 28.0% (2.69[1.38–5.26])/16.4% (1.47[0.71–3.06])/22.1% (2.06[1.09–3.88]), vs placebo 11.1%. Conjunctivitis incidence in SOLO-CONTINUE (WK36), asthma, and CRSwNP trials were low and similar among treatment groups: SOLO-CONTINUE: (qw/q2w)/ qw4qw/q8w/combined (5.4%)/4.6%/3.6%/4.7%, vs placebo 4.9%; DRI12544: WK24 300mg-q2w/300mg-q4w/200mg-q2w/200mg-q4w/combined 0%/1.3%/1.4%/2.0%/1.1%, vs placebo 1.3%; QUEST: WK52 300mg-q2w/200mg-q2w/combined 2.2%/1.3%/1.7%, vs placebo-2 mL/ placebo-1.14 mL/placebo combined 2.8%/1.9%/2.4%; VENTURE: WK24 300mg q2w 1.0%, vs placebo 0.9%; ACT12340: WK16 qw 0 vs placebo 3.3%. No patients reported conjunctivitis in the EoE trial (WK12). Conjunctivitis was mostly mild to moderate in severity and resolved/resolving by the end of the treatment period in all trials.

CONCLUSIONS: Conjunctivitis was more frequent in dupilumab-treated vs placebo patients in AD trials, except for SOLO-CONTINUE, in which patients showed low and similar rates of conjunctivitis in all treatment groups. Conjunctivitis rates in the asthma/CRSwNP/EoE trials were very low and similar among treatment groups. Most cases were mild or moderate, and resolved/resolving by the end of the treatment period.

ACKNOWLEDGMENTS: Data first presented at DERMatology Essential Resource Meeting (DERM); Las Vegas, NV, USA; July 19 – 22, 2018. Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifier: AD phase 2b (R668-AD-1021; NCT01859988), LIBERTY AD SOLO 1 (NCT02277743), LIBERTY AD SOLO 2 (NCT02277769), LIBERTY AD CHRONOS (NCT02260986), LIBERTY AD CAFÉ (NCT02755649), LIBERTY AD SOLO-CONTINUE (NCT02395133), asthma phase 2b (DRI12544; NCT01854047), LIBERTY AD QUEST (NCT02414854), LIBERTY AD VENTURE (NCT02528214), CRSwNP phase 2a (ACT12340; NCT01920893), and EoE phase 2 (R668-EE-1324; NCT02379052). Medical writing/editorial assistance provided by Vicki Schwartz, PhD, and Natalie Adlesic, PhD, of Excerpta Medica, funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

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PA-15: Diluted and Hyperdiluted Calcium Hydroxylapatite for Skin Tightening: Guidelines from a Global Consensus Panel

Dr Kate Goldie, MBChB, on behalf of the Global Consensus Panel

BACKGROUND: Approved uses of calcium hydroxyapatite (CaHA) include the correction of moderate-to-severe wrinkles and folds and correction of volume loss in the midface and dorsum of the hands. Clinicians have also begun to expand the uses of CaHA through dilution and subsdermal injection to improve skin laxity in multiple areas of the face and body.

OBJECTIVE: The goals of the present consensus guidelines were to summarize the available data and evidence for the safe and effective use of diluted CaHA, and to provide recommendations and a clear set of preliminary guidelines to aesthetic physicians for how to effectively leverage these techniques in clinical practice.

METHODS: A panel of expert aesthetic physicians from multiple international regions convened to develop a consensus on guidelines for treating laxity and superficial wrinkles using diluted–CaHA (ratio of 1:1) and hyperdiluted (≥1:2) CaHA.

RESULTS: Biostimulation is a key function of diluted and hyperdiluted CaHA. Targeted neocollagenesis can improve laxity and skin quality in several areas of the body, including the face/neck, décolletage, upper and lower extremities, abdomen, and buttocks. Superficial use of diluted/hyperdiluted CaHA can be complementary to volume augmentation with undiluted product, and may be combined with additional modalities for optimal results. Injection of diluted/hyperdiluted CaHA is well tolerated, with adverse events predominantly associated with the injection procedure itself. Great care should be exercised when used in thinner and darker skin types; in such cases, too-superficial injection of less diluted CaHA may be associated with an increased number of adverse events.

CONCLUSION: When injected more superficially in the subdermal plane in its diluted and hyperdiluted form in the mid- and lower face, neck and décolletage, upper arms, buttocks, thighs, and abdomen, CaHA appears to promote dermal remodeling through stimulation of collagen and elastin for a skin-tightening effect and to improve superficial wrinkles, elasticity, and skin thickness. Since the evidence in the literature to support this practice is limited at present, this report provides preliminary guidelines for the novel, off-label use of CaHA as a biostimulatory agent in the face and body with the expectation that future rigorous clinical trials will provide further evidence for optimal outcomes.

DISCLOSURES: Dr Goldie has been a consultant for Merz North America, Inc. This activity was sponsored by Merz North America, Inc.
PA-16: Distribution of Depression and Suicidality in a Psoriasis Clinical Trial Population

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BACKGROUND: Patients with psoriasis have an increased risk of depression and suicidal ideation and behavior (SIB).

OBJECTIVE: To assess the effect of brodalumab, a fully human anti–interleukin-17 receptor A monoclonal antibody for the treatment of moderate-to-severe psoriasis, on depression and SIB in patients participating in 3 multicenter, randomized, placebo- and active comparator–controlled phase 3 trials (AMIGANE-1/-2/-3) and one phase 2 trial.

METHODS: Rates of depression adverse events (AEs) and SIB (intentional self-injury, suicidal behavior, suicide attempt, and completed suicide) were assessed across the United States, Canada, Europe, Australia, and Russia using pooled data from one phase 2 and three phase 3 clinical trials of brodalumab in patients who received ≥1 dose of brodalumab.

RESULTS: A total of 4464 patients received brodalumab with cumulative exposure times, as follows: United States, 3680.9 patient-years (py; n=1937); Canada, 1473.5 py (n=631); Europe, 3496.3 py (n=1651); Australia, 388.9 py (n=180); and Russia, 134.4 py (n=65). Of note, the brodalumab trials had no exclusions based on the presence or history of psychiatric disorders or substance abuse. The percentages (95% CI) of long-term extension patients (LTE pts; those who continued past week 52) with depression at baseline by medical history were as follows: United States, 18.6% (16.9%-20.4%; n=360); Canada, 22.7% (19.5%-26.1%; n=143); Europe, 5.7% (4.6%-6.9%; n=94); Australia, 20.0% (14.4%-26.6%; n=36); and Russia, 0% (0%-5.5%; n=0). The percentages (95% CI) of LTE pts with SIB at baseline were as follows: United States, 2.8% (2.1%-3.7%; n=55); Canada, 3.8% (2.5%-5.6%; n=24); Europe, 1.8% (1.2%-2.5%; n=29); Australia, 6.7% (3.5%-11.4%; n=12); and Russia, 3.1% (0.4%-10.7%; n=2).

CONCLUSIONS: In contrast with other clinical trials in which patients with a history of psychiatric disorders or substance abuse were excluded, clinical trials of brodalumab were reflective of the real-world population of patients with moderate-to-severe psoriasis.

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DISCLOSURES: Steven R. Feldman has received research, speaking, and/or consulting support from AbbVie, Inc; Advance Medical, Inc; Almirall; Boehringer Ingelheim; Caremark; Celgene Corporation; Galderma; GlaxoSmithKline/Stiefel; Informa; Janssen; LEO Pharma; Eli Lilly & Co; Menlo Therapeutics Inc; Merck; Mylan; National Biological Corporation; National Psoriasis Foundation; Novan; Novartis; Ortho Dermatologics; Pfizer, Inc; Quirent Co; Regeneron; Samsung Bioepis; Suncare Research; Sun Pharmaceuticals Industries Ltd; and UpToDate. Dr Feldman consults through Gerson Lehrman Group; Guidepoint Global, LLC; and other organizations and is the founder and majority owner of www.DrScore.com and the founder and part owner of Causa Research. Susan Harris is an employee of Bausch Health and holds stock and/or stock options in the company. Abby Jacobson is an employee of Ortho Dermatologics and holds stock and/or stock options in Bausch Health. Robert J. Israel is an employee of Bausch Health and holds stock and/or stock options in the company.

FUNDING: This study was sponsored by Amgen, Inc. Medical writing support was provided by MedThink SciCom under the direction of the authors and was funded by Ortho Dermatologics.

PA-17: Dupilumab Efficacy and Safety in Adolescents with Moderate-to-Severe Atopic Dermatitis: Results from a Multicenter, Randomized, Placebo-Controlled, Double-Blinded, Parallel-Group, Phase 3 Study

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BACKGROUND: Dupilumab, a fully human anti-interleukin (IL)-4Rα monoclonal antibody that inhibits signaling of IL-4 and IL-13, key drivers of Type 2-mediated inflammation, is approved for treating adults with inadequately controlled moderate-to-severe AD. OBJECTIVE: To report the efficacy and safety of dupilumab monotherapy in a phase 3 trial in adolescents with moderate-to-severe AD inadequately controlled with topical therapies (AD-1526; NCT03054428).

METHODS: Patients (<12 to <18 years) with moderate-to-severe AD received subcutaneous dupilumab every 2 weeks (q2w; 200mg if baseline [BL] weight <60 kg; 300mg if BL weight ≥60 kg) or every 4 weeks (q4w; 300mg) or placebo (PBO) q2w, for 16 weeks. Topical or systemic AD
therapies were prohibited but allowed as rescue treatment for intolerable symptoms.

RESULTS: 251 pts were randomized: 82 to dupilumab 200 or 300mg q2w, 84 to 300mg q4w, and 85 to PBO. BL characteristics were balanced between treatment groups. At Week (Wk) 16, a significantly higher proportion of dupilumab- than PBO-treated patients (q2w/q4w vs placebo) achieved Investigator’s Global Assessment (IGA) score of 0 or 1 (24.4%/17.9% vs 2.4%; \(P < 0.0001\) ) and ≥ 75% improvement in Eczema Area and Severity Index score (EASI-75; 41.5%/38.1% vs 8.2%; \(P < 0.0001\) both). Dupilumab improved least squares mean % changes from baseline to Wk16 in EASI (~65.9%/~64.8% vs ~23.6%), peak pruritus Numerical Rating Scale (NRS) (~47.9%/~45.5% vs ~19.0%). At Wk16, more dupilumab- than placebo-treated patients achieved ≥3- or ≥4-point improvement in pruritus NRS, EASI-50, or EASI-90 (\(P < 0.0005\) for all). Dupilumab also improved scores on the Children’s Dermatology Life Quality Index and Patient-Oriented Eczema Measure (\(P < 0.0001\) for all). Numerically higher improvement in Hospital Anxiety and Depression Scale scores was seen with both dupilumab treatment groups vs PBO. A numerically higher proportion of pts used rescue medications in the PBO vs dupilumab groups, and in the q4w vs q2w dupilumab group. Steady-state mean trough concentrations were approximately 3-fold higher with dupilumab q2w vs q4w. Incidence of treatment-emergent adverse events were similar in all treatment groups. Rates of AD exacerbation and non-herpetic skin infections were numerically higher with PBO vs dupilumab; conjunctivitis and injection-site reactions were more common with dupilumab vs PBO. These events were not serious or severe.

CONCLUSIONS: Dupilumab showed clinically meaningful and statistically significant improvements in AD signs and symptoms (including pruritus) and QoL in adolescents with moderate-to-severe AD with an acceptable safety profile. Both PBO-corrected efficacy and safety of dupilumab in adolescent pts were similar to those in adults.


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PA-18: Effects of Brodalumab on Anxiety and Depression in Patients with Psoriasis and Moderate-to-Severe Anxiety and Depression: Results from a Phase 3, Randomized, Controlled Clinical Trial

Leon Kirck1, April Armstrong2, Benjamin Ehst3, Roger S. Ho4, Abby Jacobson1
BACKGROUND: Anxiety and depression occur more frequently among patients with psoriasis than in the general population. Treatment of psoriasis may reduce mental health comorbidities. Brodalumab is a fully human monoclonal antibody that targets interleukin-17 receptor A, antagonizing inflammatory cytokines involved in psoriasis pathogenesis, and has demonstrated efficacy in the treatment of plaque psoriasis.

OBJECTIVE: The objective of this post hoc subgroup analysis was to evaluate changes in anxiety and depression in patients receiving brodalumab.

METHODS: In this 52-week phase 3 clinical trial, adult patients with moderate-to-severe plaque psoriasis were randomized to brodalumab (140 or 210 mg) every 2 weeks (Q2W) or placebo during a 12-week induction phase. At week 12, patients receiving brodalumab who did not achieve treatment success (static physician’s global assessment score ≤1, equating to clear or almost clear skin) and patients receiving placebo were allocated to treatment with brodalumab 210 mg Q2W (US food and Drug Administration–approved dose) for the remaining 40 weeks. Patients receiving brodalumab who achieved treatment success at week 12 were re-randomized to the same dose of brodalumab or placebo. Hospital anxiety and depression scale (HADS) scores are reported for baseline and weeks 12 and 36 on the basis of data availability. The HADS questionnaire consists of 7 items individually answered each for anxiety and depression on a 4-point scale, where response categories range from 0 to 3 (range for all 7 items, 0–21). A HADS score ≥11 is considered “moderate to severe.” Patients in this analysis were stratified by HADS anxiety or depression score at baseline and weeks 12 and 36 on the basis of data availability. This post hoc analysis was to evaluate changes in anxiety and depression in patients receiving brodalumab.

RESULTS: At baseline, the mean (standard deviation) HADS anxiety score was 6.6 (4.1) and HADS depression score was 5.3 (4.1) among all patients in AMAGINE-1 (N=661). At baseline, 16% of patients had moderate-to-severe anxiety and 12.4% had moderate-to-severe depression. After 12 weeks of the study, patients who switched from placebo to brodalumab 210 mg Q2W (n=204) had a mean (standard error [SE]) HADS anxiety score of 6.2 (0.3) and HADS depression score of 5.4 (0.3), which improved to 4.9 (0.3) and 3.5 (0.3), respectively, at week 36. Patients with moderate-to-severe anxiety at baseline who switched from placebo to brodalumab 210 mg Q2W (n=20) had a mean (SE) HADS depression score of 12.0 (0.9) at week 12, which improved to 8.8 (1.3) at week 36. In contrast to this improvement seen with brodalumab treatment, a trend toward worsening in HADS scores was observed in patients treated with an initial 12 weeks of brodalumab 210 mg Q2W who were then re-randomized to placebo.

LIMITATIONS: The generalizability of these data is limited because of small sample sizes in some patient groups.

CONCLUSION: This post hoc analysis of subgroups from the AMAGINE-1 randomized trial suggests that brodalumab may reduce the burden of mental health comorbidities associated with psoriasis such as anxiety and depression.

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FUNDING: This study was sponsored by Ortho Dermatologics. Medical writing support was provided by MedThink SciCom under the direction of the authors and was funded by Ortho Dermatologics.

DISCLOSURES: Leon Kircik has served as an investigator, speaker, advisory board member, or consultant for AbbVie, Aclaris, Allergan, Amgen, Anacor, Assos, Astellas, Asubio, Bausch Health, Berlex (Bayer Healthcare), Biogen Idec, BioLife, Biopelle, Boehringer Ingelheim, Breckenridge, Celgene, Centocor, ColBar, CollaGenex, CombiMatrix, Connetics, Coria, Dermik Laboratories, Dermira, Dow Pharmaceutical Sciences, DUSA, Eli Lilly, Embil, EOS, Ferndale Laboratories, Galderma Laboratories, Genentech, GlaxoSmithKline, Health Point, IDERA, Innocutis Medical, Innovail, Intendis, Johnson & Johnson, Laboratory Skin Care, Leo, L’Oreal, 3M, Maruho Co, Medical International Technologies, Medicis, Merck & Co, Merz, Nano Bio Corporation, Novartis, Noven, Nucryst, Obagi Medical Products, Onset, OrthoNeutrogena, PediaPharma, Promius, PharmaDerm, Pfizer, PuraCap, QLT, Quatrix, Quinova, Serono (Merck-Serono International SA), SkinMedica, Stiefel Laboratories, Sun Pharma, Taro, TolerRx, Triax, UCB, Warner-Chilcott, XenoPort, and ZAGE. April Armstrong has been a research investigator for and consultant to AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Pfizer, Regeneron, Sanofi, Leo, Modernizing Medicine, Science 37, and/or Ortho Dermatologics. Benjamin Esh has received speaker fees from Regeneron/Sanofi-Genzyme, Novartis, and Eli Lilly; received advisory board consulting fees from Novartis, Eli Lilly, and Janssen; served as an investigator for Novartis, Eli Lilly, Janssen, Merck, Sun Pharma, Bristol-Myers Squibb, Dermira, BI, Pfizer, Leo, Regeneron, AbbVie, UCB, Sienna, Vidak, Aclaris, and Allergan; and served as the principal investigator for Amgen-sponsored clinical trials of brodalumab. Roger S. Ho has attended advisory boards for Ortho Dermatologics and Cutanea. Abby Jacobson is an employee of Ortho Dermatologics and may hold stocks and/or stock options in Bausch Health.
PA-19: Efficacy and Safety of FMX103 (1.5% Minocycline Foam) in the Treatment of Moderate-to-Severe Papulopustular Rosacea: Results from Two Phase 3 Randomized, Multicenter, Double-Blind, Vehicle-Controlled Studies

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OBJECTIVE: To determine the efficacy, safety, and local tolerability of FMX103 1.5% topical minocycline foam used for 12 weeks in the treatment of papulopustular rosacea.

METHODS: Two Phase 3, randomized, multicenter, double-blind, vehicle-controlled, 2-arm studies (Study FX2016-11 and Study FX2016-12) were conducted in subjects of ≥18 years of age with moderate-to-severe papulopustular rosacea. Subjects were randomized 2:1 to either FMX103 or vehicle treatment, respectively, and applied, or had applied for them, FMX103 foam or vehicle foam once daily to the face for 12 weeks. They were evaluated at baseline and weeks 2, 4, 8, and 12. Co-primary efficacy end points were absolute change from baseline in inflammatory lesion count and the proportion of subjects with treatment success, defined as an Investigator’s Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with a ≥2-grade improvement from baseline at week 12. Safety evaluations included adverse events, vital signs, physical examination, laboratory investigations, and local tolerability assessment. Subject global assessment (SGA) and subject satisfaction were assessed by a questionnaire at week 12.

RESULTS: A total of 1522 subjects were enrolled in the 2 studies (Study FX2016-11, n=751; Study FX2016-12, n=771). At baseline, in Study FX2016-11 and FX2016-12, respectively, the mean inflammatory lesion count was 28.5 and 30.0 for the FMX103 treatment groups, and 29.0 and 30.2 for the vehicle treatment groups. Both studies met both co-primary end points. There were statistically significant reductions in number of inflammatory lesions from baseline with FMX103 (Study FX2016-11, −17.57 vs −15.65, P=.003; Study FX2016-12, −18.54 vs −14.88; P<.0001) and significantly higher rates of IGA treatment success vs vehicle (Study FX2016-11, 52.1% vs 43.0%, P=.027; Study FX2016-12, 49.1% vs 39.0%, P=.008). The most common treatment-emergent adverse event (TEAE) for both studies was upper respiratory tract infection. There were no serious treatment-related TEAEs. Overall, 9 subjects across both studies discontinued due to a TEAE (FMX103, 7 subjects; vehicle, 2 subjects).

CONCLUSION: FMX103 appeared to be effective with a favorable safety profile for the treatment of moderate-to-severe papulopustular rosacea.

DISCLOSURES: This study was funded by Foamix Pharmaceuticals. Dr Linda Stein Gold, Dr James Q. Del Rosso, Dr Neal D. Bhatia, Dr Deidre Hooper, and Dr Walter Nahm served as investigators for Foamix. Dr Iain Stuart is an employee of Foamix Pharmaceuticals.

PA-20: Efficacy and Safety of Apremilast in Patients with Moderate to Severe Plaque Psoriasis of the Scalp: Results of a Phase 3, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study

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BACKGROUND: Many patients with psoriasis report that they are most bothered by symptoms in difficult-to-treat, highly visible, and pruritic areas, such as the scalp. Topical therapies can be difficult to apply to the scalp area.

OBJECTIVE: We evaluated the efficacy and safety of apremilast, an oral PDE4 inhibitor indicated for the treatment of moderate to severe plaque psoriasis, in patients with moderate to severe psoriasis of the scalp.

METHODS: This was a phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled study in patients with moderate to severe plaque psoriasis of the scalp (scalp Physician Global Assessment [SCPGA] ≥3 [moderate or greater]; psoriasis-involved scalp surface area [SSA] ≥20%) who also had moderate to severe plaque psoriasis (PASI ≥12, psoriasis-involved BSA ≥10%; static PGA [SPGA] ≥3 [moderate or greater]) and an inadequate response or intolerance to ≥1 topical therapy for plaque psoriasis of the scalp. Patients were randomized (2:1) to apremilast 30 mg BID (APR) or PBO for the PBO-controlled phase through Week 16 and then continued or switched to APR for treatment through Week 32. The primary endpoint was the proportion of patients achieving SCPGA response at Week 16 (score of 0 [clear] or 1 [almost clear] with ≥2-point reduction from baseline) with APR vs PBO. Secondary endpoints included the proportion of patients with ≥4-point improvement from baseline in whole body itch and scalp itch NRS scores and change...
from baseline at Week 16 in DLQI total score. Analyses were performed using the Cochran-Mantel-Haenszel method for binary endpoints and analysis of covariance model for continuous endpoints with missing values imputed using the multiple imputation (MI) method. For the primary endpoint, sensitivity analyses were also performed using the last-observation-carried-forward (LOCF) and nonresponder imputation (NRI) methods.

**RESULTS:** A total of 303 patients were randomized (APR n=201, PBO n=102). Baseline demographics were generally comparable between APR and PBO groups (mean [SD] age, 47.0 [15.0] and 46.7 [15.2] years; mean [SD] disease duration, 15.7 [12.4] and 14.8 [11.3] years). At baseline, mean (SD) values for APR and PBO, respectively, were as follows: SSA, 61.9% (27.2) and 58.2% (26.4); scalp itch NRS, 6.6 (2.5) and 6.7 (2.4); BSA, 19.0% (10.8) and 21.2% (14.8); whole body itch NRS, 7.2 (2.3) and 7.2 (2.0); and DLQI, 12.6 (7.0) and 12.6 (7.2). In all, 252 patients completed the PBO-controlled phase (APR, 168/201 [83.6%]; PBO, 84/102 [82.4%]). The most frequently cited reasons for discontinuation included withdrawal by patient (7.3%), AEs (3.6%), and lack of efficacy (2.3%). At Week 16, significantly more patients treated with APR vs PBO achieved the primary endpoint (43.4% vs 13.8%, \( P < 0.0001 \)). Results from sensitivity analyses comparing APR vs PBO using LOCF and NRI were consistent with MI results for the primary endpoint (LOCF: 40.3% vs 13.7%, \( P < 0.0001 \); NRI: 38.8% vs 10.8%, \( P < 0.0001 \)). In addition, in patients treated with APR, 47.0% and 45.3% achieved ≥4-point improvement from baseline in scalp itch and whole body itch NRS scores vs 21.3% and 22.5% of patients treated with PBO (\( P = 0.0001 \) for both comparisons). Statistically significant improvements with APR vs PBO were observed on both itch NRS measures as early as Week 2 (scalp: 26.0% vs 11.5%; whole body: 20.5% vs 3.5%; \( P < 0.01 \) and \( P < 0.0001 \), respectively). Improvement from baseline in DLQI score at Week 16 was significantly greater with APR vs PBO (least-square means, −7.1 vs −4.2, \( P < 0.0001 \)). During the PBO-controlled period, the proportion of patients with ≥1 AE was 66.5% with APR and 48.0% with PBO, and the most common AEs, occurring in ≥5% of patients in either treatment group, were diarrhea (30.5% and 10.8%), nausea (21.5% and 5.9%), headache (11.5% and 4.9%), and vomiting (5.5% and 2.0%) with APR and PBO, respectively.

**CONCLUSION:** Findings demonstrated the efficacy of APR in patients with moderate to severe psoriasis of the scalp. AEs were consistent with the known safety profile of apremilast.

**PA-21: Efficacy and Safety of Ixekizumab in Patients with Active Psoriatic Arthritis and Previous Inadequate Response to TNF inhibitors: 52-Week Results from a Phase 3 Study**

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**BACKGROUND:** Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. In patients with active psoriatic arthritis (PsA) who had an inadequate response to tumor necrosis factor inhibitors (TNFi), IXE was superior to placebo (PBO) in improving the signs and symptoms of PsA after 24 weeks of treatment (SPIRIT-P2; NCT02349295).

**OBJECTIVE:** The objective of this study is to report the Week 52 interim efficacy and safety findings of IXE treatment during the Extension Period (EP) of SPIRIT-P2 (Weeks 24-156).

**METHODS:** SPIRIT-P2 is a phase 3, multicenter, double-blind study. All 363 patients had an inadequate response to one or two TNFi or were intolerant to TNFi. During the Double-Blind Treatment Period (DBTP; Weeks 0-24), patients were randomly assigned 1:1:1 to subcutaneous administration of either 80 mg IXE every 4 weeks (Q4W; N=122) or every 2 weeks (Q2W; N=118) following a 160 mg starting dose at Week 0, or PBO (N=118). Of these, 310 patients completed the DBTP and entered the EP (Weeks 24-156). Patients randomized to IXE at Week 0 continued the same dose regimen in the EP. PBO patients were re-randomized (1:1) to IXE Q4W or Q2W at Week 16 (inadequate responders) or 24. In this interim analysis, efficacy (up to Week 52) and safety (up to Week 156) were analyzed using the EP population, defined as all patients who received at least 1 dose of study drug in the EP. Missing values were considered non-response for categorical data and were imputed by modified baseline observation carried forward for continuous data.

**RESULTS:** In the DBTP, a significantly higher percentage of patients achieved ACR20 at Week 24 with IXE Q4W (53%) or Q2W (48%) than with PBO (20%). For patients who entered the EP, the mean age was 52 years, 47% were male, the mean time since PsA onset was 12 years, and mean tender and swollen joint counts at baseline (Week 0) were 23 and 12, respectively. For EP patients who were initially randomized to IXE Q4W or Q2W during the DBTP, ACR20 responses at Week 52 were 68% and 59%, respectively. For patients treated with PBO during the DBTP and re-randomized to IXE Q4W or Q2W during the EP, ACR20 responses at Week 52 were 61% and 50%, respectively. The majority of adverse events (AEs) in the EP were mild or moderate in severity. Serious AEs occurred in 15 patients, and one death occurred in the EP population: a myocardial infarction in a PBO/IXE Q2W patient 502 days after starting IXE.

**CONCLUSIONS:** IXE demonstrated sustained improvement in the signs and symptoms of PsA across treatment...
groups during the EP. The safety profile of IXE observed in the EP population was consistent with the safety profile of the intent-to-treat population in the DBTP of SPIRIT-P2.

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**PA-22: Efficacy of Ixekizumab in Patients Previously Treated with IL-17 Inhibitors**

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**BACKGROUND/OBJECTIVES:** Previous exposure to biologics is thought to potentially impact efficacy of subsequent biologic therapies. In this analysis of a phase 3b clinical trial of ixekizumab, an IL-17A antagonist, we evaluated the impact of previous use of biologics, particularly those targeting the IL-17 pathway (brodalumab [IL-17 receptor A antagonist] or secukinumab [IL-17A antagonist]), on 52-week efficacy in patients with moderate-to-severe psoriasis.

**METHODS:** In this phase 3b, multicenter, randomized, double-blind, parallel-group trial (IXORA-P, NCT02513550), patients with moderate-to-severe plaque psoriasis were randomized at a 1:1:1 ratio to three dosing regimens of IXE 80 mg: IXE Q2W (N=611), IXE Q4W (N=310), or IXE Q4W/IXE Q2W step-up (N=306), each with a starting dose of 160 mg. IXE 4QW to IXE Q2W step up was determined by predefined criteria to which investigators were blinded. Patients were excluded if they had previously failed to respond to an IL-17 inhibitor, per investigator assessment. Improvements in the Psoriasis Area and Severity Index of 75%, 90%, and 100% (PASI 75, PASI 90, and PASI 100) responses were summarized in the EP population was consistent with the safety profile of ixekizumab through 52 weeks of treatment.

**RESULTS:** At study entry, among patients treated with IXE Q2W, IXE Q4W, and IXE Q4W/IXE Q2W step-up, 297 (48.6%), 144 (46.5%), and 131 (42.8%) respectively, had previously been treated with a biologic therapy, and 148 (24.2%), 64 (21.6%), and 73 (23.9%) respectively, had been previously treated with a biologic targeting the IL-17 pathway (brodalumab [22.6%] or secukinumab [1.1%]). At 52 Weeks, PASI 75, 90, and 100 response rates were similar for patients who were naïve to any biologic therapy and patients who were biologic experienced, regardless of dosing group. Furthermore, PASI 75 response rates for IL-17 inhibitor-naive and IL-17 inhibitor-experienced patients were 85% and 89%, 79% and 81%, and 83% and 85%, respectively, in patients treated with IXE Q2W, IXE Q4W, and IXE Q4W/IXE Q2W step-up. PASI 90 response rates for IL-17-inhibitor naïve and IL-17-inhibitor experienced patients were 79% and 82%, 65% and 67%, and 73% and 75%, respectively, in patients treated with IXE Q2W, IXE Q4W, and IXE Q4W/IXE Q2W step-up. PASI 100 response rates for IL-17-inhibitor naïve and IL-17-inhibitor experienced patients were 60% and 59%, 44% and 42%, and 49% and 52%, respectively, in patients treated with IXE Q2W, IXE Q4W, and IXE Q4W/IXE Q2W step-up. There were no statistically significant interactions between dosing regimen and previous IL-17 inhibitor use for any of these outcomes.

**CONCLUSIONS:** Neither prior exposure to any biologic nor to brodalumab or secukinumab impacted efficacy of ixekizumab through 52 weeks of treatment.

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**PA-23: Efficacy of Risankizumab Compared with Placebo Across Subgroups in Patients with Moderate-to-Severe Plaque Psoriasis: Integrated Analyses from Three Phase 3 Trials**

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**INTRODUCTION:** Interleukin-23 (IL-23) plays a key role in the development and maintenance of psoriatic lesions by regulating multiple effector cytokines. Risankizumab (RZB) is a humanized IgG1 monoclonal antibody that selectively inhibits IL-23 by binding to its p19 subunit. The superior efficacy of RZB compared with placebo (PBO) as well as acceptable safety and tolerability profile have been demonstrated in three independent phase 3 randomized, double-blind, PBO-controlled trials. The objective of this analysis was to evaluate the integrated efficacy of RZB compared with PBO across subgroups of patients (pts) with moderate-to-severe plaque psoriasis.

**MATERIALS/METHODS:** Data from three phase 3 studies in pts with moderate-to-severe plaque psoriasis were integrated over the 16-week (wk) PBO-controlled period. Pts stratified by weight and prior TNFi-exposure at
randomization received either 150 mg RZB (N=1005) at wks 0 and 4 or matched PBO (N=300). Co-primary efficacy endpoints assessed for consistency at wk 16 across subgroups were PASI 90 and sPGA 0/1 responses. Missing data were imputed as non-responders. Treatment comparisons were conducted by Cochran-Mantel-Haenszel test stratified by study, baseline weight (≤100 kg vs >100 kg), and prior exposure to TNFi (0 vs ≥1).

RESULTS: Among 1305 pts included in this integrated analysis, baseline demographics and disease characteristics were generally similar between the two treatment arms. Mean age was 48.1 years and mean weight was 90.8 kg; 70.3% of pts were male. Mean baseline PASI and BSA were of 20.3 and 26.1%, respectively. Median baseline PASI score was 18.0, while baseline sPGA was moderate in 80.2% of pts. A history of diagnosed or suspected PsA was reported in 30.9% of pts. At wk 16, RZB-treated pts achieved significantly higher PASI 90 and sPGA 0/1 response rates compared with PBO-treated pts (P<0.001 for both endpoints across all subgroups; regardless of baseline demographics or disease characteristics. The efficacy of RZB in each of the subpopulations was comparable to the overall efficacy in the pooled population.

CONCLUSION: Treatment with RZB was associated with superior efficacy compared with PBO in adult pts with moderate-to-severe plaque psoriasis, regardless of baseline demographics or disease characteristics.

DISCLOSURES: M Lebwohl has received grants as an investigator from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Biotech, Kadmon Corporation, LEO Pharma, MedImmune, Novartis, Sun Pharma, and Valeant, and has been a paid consultant for Boehringer Ingelheim and Leo Pharma. PD Ghislain has received honoraria from AbbVie, Amgen, Celgene, Janssen, Leo, Pfizer, Novartis, and Stiefel. C Lynde has received honoraria from AbbVie, Amgen, BMS, Celgene, Eli-Lilly, Flen, Calderma, Janssen, Leo, Marin, Meda, Menarini, MSD, Novartis, Pfizer, and UCB for participation as a consultant, investigator, speaker, and for participation on ad boards. F Kerdel has received honoraria from AbbVie, Amgen, Celgene, Janssen, Leo, Pfizer, Eli Lilly, Novartis, and Stiefel for participation as a speaker; and received grants from AbbVie, Amgen, AstraZeneca, Celgene, Janssen, Eli Lilly, Novartis, and Pfizer for participation as an investigator. Y Gu, JM Valdes, and EZH Thompson are full-time employees of AbbVie and may own stock/options. C Lynde has received honoraria as a principal investigator, speaker, and/or consultant from AbbVie, Amgen, Boehringer Ingelheim, Eli Lilly, Janssen, Merck, Novartis, and Valeant.

ACKNOWLEDGMENTS: AbbVie and Boehringer Ingelheim funded the UltIMMa-1 (NCT02684370), UltIMMa-2 (NCT02684357), and IMMhance (NCT02672852) studies; Boehringer Ingelheim contributed to its design and participated in data collection, AbbVie performed the data analysis, and participated in interpretation of the data, and both participated in writing, review, and approval of the abstract. AbbVie, Boehringer Ingelheim, and the authors thank all study investigators for their contributions and the patients who participated in this study. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

PA-24: Efficacy, Safety, and Durability of Collagenase Clostridium Histolyticum for the Treatment of Edematous Fibrosclerotic Panniculopathy (Cellulite)

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BACKGROUND: Multiple topical agents or techniques have been considered to reduce the appearance of cellulite in women. However, well-designed clinical trials using validated cellulite severity scales are generally lacking. Collagenase clostridium histolyticum (CCH) subcutaneous injection was shown to be safe and efficacious for cellulite in women in a phase 2a, randomized, placebo-controlled trial (RCT). In addition, a phase 2b RCT assessed the efficacy of CCH in women with moderate to severe cellulite using the Clinician Reported Photonumeric Cellulite Severity Scale (CR-PCSS) and the Patient Reported Photonumeric Cellulite Severity Scale (PR-PCSS). CCH significantly improved the appearance of cellulite versus placebo based on both clinician and patient ratings using these validated scales.

OBJECTIVES: To evaluate the safety and durability of CCH for correction of cellulite-related contour alterations.

METHODS: The current study was an open-label extension of the phase 2b RCT. Adult women completing the RCT could enroll in the observation phase or, if they had a right/left buttck or posterolateral thigh area with moderate/severe cellulite (CR-PCSS and PR-PCSS scores of 3-4 and Hessell Cellulite Severity Scale score ≤13), could have the area treated with CCH (first treatment [RCT placebo group], new area, area retreatment) after RCT unblinding. The women received CCH 0.84 mg/session during 3 sessions (Days 1, 22, and 43). Cellulite severity and safety were assessed on Days 22, 43, 71, and then every 3 months for ≥1 year after first CCH exposure for each treated area. Post-baseline improvements in CR-PCSS and PR-PCSS were evaluated at Day 71 in the RCT.

RESULTS: 259 women from the RCT were enrolled: 53 (based on Day 71 data) were RCT ≥1-level composite responders (ie, ≥1-level improvement in both CR-PCSS and PR-PCSS) and followed for durability of response; 200 received open-label CCH (56.0% of which were first treatments with CCH). For evaluable ≥2-level composite responders (ie, 2-level improvement in both CR-PCSS and PR-PCSS in RCT), durable response (ie, no return to baseline or worse at ≥2 consecutive visits) was observed in 100% of patients at 180 days (19 of 19 patients) and 360 days (16 of 16 patients) post-treatment. Six women treated with open-label CCH discontinued due to...
an adverse event. Common adverse events were injection-site bruising and pain.

LIMITATIONS: Limitations included the open-label study design and the small sample of women with available durability data at 180 and 360 days post-treatment.

CONCLUSIONS: CCH treatment met the primary efficacy endpoints, was generally well tolerated, and provided durable improvement in cellulite appearance.

FUNDING: Endo Pharmaceuticals Inc.

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DISCLOSURES: JK reports no conflicts to disclose. LSB reports being an advisory board participant for Endo Pharmaceuticals Inc. and Merz North America; being a clinical investigator for Endo Pharmaceuticals Inc.; and serving as a consultant for Viveve. QX and MPM are employees of Endo Pharmaceuticals Inc. MTK is a former employee of Endo Pharmaceuticals Inc.

PA-25: Environmental Protection and Rejuvenation From a Novel Antioxidant Dual Serum System: A Randomized, Double-Blind, Regimen Controlled, Multi-Center Study

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Traditionally, UV rays have been the focus of external factors that contribute to the aged appearance of the skin. Increasing research has shown that other environmental factors such as air pollution also contribute to skin damage. A novel antioxidant dual serum system (LVS), consisting of a DAY serum (LVD) and a NIGHT serum (LVN), was developed to provide targeted protective and reparative effects by combining a unique blend of antioxidants and peptides.

A 12-week, double-blind, randomized, regimen-controlled, multi-center study was conducted to assess the efficacy and tolerability of LVS on subjects presenting with moderate to severe photo-damage, and who live in an urban area with low/moderate air quality. 61 female subjects aged 36 to 65 years and Fitzpatrick Skin Type I-VI completed the study (Active=40, Control=21). The active group received LVS (LVD applied once daily in the morning and LVN applied once daily in the evening) and a basic skincare regimen (cleanser, moisturizer, and SPF 35 sunscreen). The control group received the same basic skincare regimen. Visits occurred at baseline and weeks 4, 8, and 12. Clinical grading (radiance, overall photo-damage, tactile and visual skin roughness, global fine and coarse lines/wrinkles, skin tone evenness, and crow’s feet

LVS “improved the radiance of my skin,” and “improved overall photo-damage (week 12; p≤0.04; Wilcoxon rank-sum test), tactile roughness (week 12; p=0.05; Wilcoxon rank-sum test), and global fine lines/wrinkles (week 12; p=0.02; Wilcoxon rank-sum test). Biopsy results, skin swab analysis, and standardized photographs support the clinical grading findings. At all follow-up visits, LVS was consistently highly rated over control by subjects, with a significant proportion of subjects agreeing at week 12 that LVS “improved the radience of my skin,” and “improved the overall health and look of my skin” (all p≤0.045; Fisher’s exact test).

Results from this study suggest that LVS may provide essential protection and reparative effects to skin exposed to the damaging effects of environmental factors.

PA-26: Escalating Doses of IncobotulinumtoxinA for Extended Treatment of Glabellar Frown lines: Safety and Efficacy Results from a Randomized, Double-Blind Study

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BACKGROUND: The effect of escalating doses of incobotulinumtoxinA (≥20U for glabellar frown lines [GFL]) on response rates and duration of response has not been studied. Previously, analysis of a pilot study suggested a roughly linear relationship to duration of response with doses escalating in 20U increments.

OBJECTIVE: In this study, the effect of varying doses of incobotulinumtoxinA on the safety, efficacy, and duration of treatment effect for GFL was assessed.

METHODS: Subjects (N=37) with moderate to severe GFL (Merz Aesthetics Scales [MAS]) were randomized to receive 1 of 3 doses: 20U (control; n=8), 60U (n=11), and 100U (n=17). The mean time to return to baseline for mean MAS scores (at maximum frown) was used to assess duration of response. Subjects with a ≥2-point improvement in wrinkle severity at maximum contraction were also assessed over time.

RESULTS: A strong dose response was observed for clinical efficacy and duration of effect. An increase in the duration of effect was noted with higher doses; mean scores returned to baseline at ~4 months (20U), ~7 months (60U), and ≥11 months (100U). Treatment response was highest in the 60U and 100U dose groups, by 9 months, 23% of those in the 100U group remained responders. Overall subject satisfaction was high. All AEs (19 total in 14 subjects)
were consistent with previous incobotulinumtoxinA studies, and none were considered related to distant spread of toxin. A somewhat higher incidence of AEs was noted in the 100U dose group (47% of subjects) compared with other groups (25-36% of subjects).

CONCLUSIONS: Within the range of doses examined, there was a roughly linear relationship between incobotulinumtoxinA dose and duration of treatment effect. Safety of incobotulinumtoxinA at higher doses was favorable, with no unexpected safety findings. Overall, findings suggest that the dose of incobotulinumtoxinA for GFL can be safely increased from the standard 20U to help achieve patients’ treatment goals, including duration of effect.

DISCLOSURES: Dr Maas has served as consultant and investigator for Merz North America, Inc. This study was sponsored by a grant from Merz North America, Inc.

PA-28: FMX101 4% Topical Minocycline Foam for the Treatment of Moderate to Severe Acne Vulgaris: Efficacy and Safety from a Phase 3, Randomized, Double-Blind, Vehicle-Controlled Study

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BACKGROUND: Acne vulgaris (AV) is a prevalent chronic, inflammatory skin disorder that affects most of the population at some point in their life. FMX101 4% is a novel, stable, topical foam formulation of minocycline that has been shown to be an effective and well-tolerated treatment for acne in 2 previous double-blind Phase 3 pivotal studies (Study 04, Study 05).

OBJECTIVES: To further evaluate the efficacy and safety of daily topical administration of FMX101 4% as compared with foam vehicle for a period of 12 weeks in the treatment of moderate-to-severe AV.

METHODS: A 12-week multicenter, randomized (1:1), double-blind, vehicle-controlled study of subjects aged ≥9 years with moderate-to-severe AV (Study 22) was conducted. Subjects self-applied FMX101 4% or foam vehicle daily for 12 weeks and were evaluated at weeks 3, 6, 9, and 12. The coprimary end points were the absolute change from baseline in inflammatory lesion count and the proportion of subjects with an Investigator’s Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with ≥2 grades of improvement at week 12. A secondary endpoint was the absolute change from baseline in non-inflammatory lesion count at week 12. Safety evaluations included adverse events, vital signs, skin assessment, and laboratory investigations.

RESULTS: Of the 1507 subjects enrolled, 1293 completed the study. At 12 weeks, subjects treated with FMX101 4% showed statistically significantly greater reductions in the number of inflammatory lesions from baseline (~16.93 vs ~13.40; 95% confidence interval [CI], 2.46–4.83; P<.0001) and achieved a greater rate of IGA treatment success (30.80% vs 19.63%; P<.0001; 95% CI, 1.32–1.88) than the foam vehicle group; hence, both coprimary end points were met. FMX101 4% was also superior to vehicle foam at reducing the absolute number of non-inflammatory lesions from baseline to week 12 (~18.80 vs ~15.89,
respectively; \( P < .05 \). The most common treatment-emergent adverse events (TEAEs) included respiratory tract infection, acne, headache, influenza, and increased creatine phosphokinase, but were not treatment related. Few TEAEs led to study discontinuation (FMX101 4%, \( n = 4 \); vehicle, \( n = 3 \)). No serious treatment related TEAEs (FMX101 4%, \( n = 1 \); vehicle, \( n = 4 \)) were reported.

**CONCLUSIONS:** FMX101 4% topical minocycline foam is effective, safe, and well tolerated for the treatment of moderate-to-severe AV.

**DISCLOSURES:** This study was funded by Foamix Pharmaceuticals. Dr Joseph Raof, Dr Deirdre Hooper, Dr Martin Zaiac, Dr Tony Sullivan, and Dr Edward Lain served as investigators for Foamix. Dr Angela Moore is an investigator, consultant, and/or speaker for Abbvie, Aclaris, Actavis, Astellas, Asubio, Biofrontera, Boehringer Ingelheim, Bristol-Myers Squibb, Centocor, Coherus, Dermavant, Dermira, Eli Lilly, Foamix, Galderma, Incyte, Janssen, Leo, Mayne, Novartis, Parexel, Pfizer, Therapeutics, Verrica. Dr Leon Kirck is an investigator and consultant for Foamix. Dr Jasmina Jankic is a consultant for Foamix Pharmaceuticals. Dr Iain Stuart is an employee of Foamix Pharmaceuticals.

### PA-29: Further Analysis of Initial Non-Responders to Ixekizumab Regarding Patient Characteristics and Long-Term Outcomes

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**BACKGROUND:** The efficacy and safety of ixekizumab 80mg every 2 weeks (IXEQ2W) or every 4 weeks (IXEQ4W) has been investigated in three phase 3 trials of patients with moderate-to-severe plaque psoriasis (UNCOVER-1 [NCT01474512], UNCOVER-2 [NCT01597245], and UNCOVER-3 [NCT01646177]). Co-primary endpoints were the percentage of patients who achieved a score on the static Physicians Global Assessment (sPGA) of 0 (clear) or 1 (minimal psoriasis) and a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at week 12.

**OBJECTIVE:** This analysis determined longer-term outcomes and examined characteristics of patients who had not initially responded to induction treatment with IXEQ2W at week 12.

**METHODS:** In UNCOVER-1 and UNCOVER-2, patients who were non-responders to IXEQ2W at week 12 (sPGA ≥2 and PASI <75) received treatment with IXEQ4W to week 60. Following week 12 in the UNCOVER-3 trial, all patients, including those retrospectively identified to meet the same criteria for non-response, entered a long-term extension period during which they received IXEQ4W to week 60. Data were pooled, with patient characteristics and treatment outcomes reported for the subgroup of patients who did not respond (sPGA ≥2 and PASI <75) to IXEQ2W during the 12-week induction phase of the 3 studies and were assigned to treatment with IXEQ4W. Response parameters include PASI 75, PASI 90, PASI 100, sPGA, and absolute PASI ≤2 and ≤5 at weeks 24 and 60 (non-responder imputation; NRI).

**RESULTS:** At week 12, the pooled proportion of patients with PASI 75 response was 88.7% in the IXEQ2W treatment group. There were 73 patients who did not initially respond to IXEQ2W who then received IXEQ4W. Baseline characteristics for this group were comparable to the overall population from the 3 studies, except for bodyweight; 24/49 (49%) with data were <100kg and 25/49 (51%) were ≥100kg (IXEQ2W initial non-responders) compared with 69.1% and 30.9% (overall population). By week 24, 26 non-responders at week 12 (35.6%) had PASI 75 response; by week 60, 28 (38.4%) had PASI 75 response. Other responses observed at week 24 were also maintained up to week 60.

**CONCLUSIONS:** The proportion of patients with bodyweight over 100kg was higher for the initial non-responders vs the overall population. Approximately one third of patients who do not show a response to IXEQ2W after 12 weeks of induction therapy may show a response (PASI 75 or absolute PASI ≤5) by 24 week of maintenance therapy with IXEQ4W. Responses seen in a range of parameters can be maintained with treatment for up to 60 weeks. These findings support the continuation of ixekizumab therapy up to 24 weeks in patients who have not initially responded by week 12.

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### PA-30: Human Pharmacokinetics of Subcutaneous Collagenase Clostridium Histolyticum and Preclinical Safety of Inadvertent Intravenous Administration

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BACKGROUND: There are currently no US Food and Drug Administration–approved products available for reducing cellulite to improve the aesthetic appearance of skin. Clostridium collagenase histolyticum (CCH) is an injectable agent being evaluated in women as a treatment for cellulite that disrupts subcutaneous septae by lysing collagen and reducing cellulite or skin dimpling to achieve a skin-smoothing effect. CCH has localized action at the injection site and does not require systemic exposure for efficacy.

OBJECTIVES: To evaluate human pharmacokinetics (PK) and safety of single-dose CCH and preclinical toxicity after inadvertent intravenous (IV) dosing in rats.

METHODS: In the rat study, animals (10-15 per sex/dose) received 0, 0.029, 0.13, or 0.29 mg/dose of CCH IV every other day for 16 days (total, 8 doses) and were evaluated for gross histopathologic changes. In 2 human PK studies, 29 women received a single session of 12 subcutaneous injections per area (thigh/buttock) in 1 (n=11; total CCH dose, 0.84 mg) or 2 (n=18; total CCH dose, 1.68 mg) areas in 1 session. Blood samples were taken at baseline, 5, 10, 20, and 30 min, and at 1, 2, 4, 8, 12, 24, 48, 168, and 504 h postdose.

RESULTS: In the rat IV study, in which CCH 0.29 mg, 96× human equivalent dose (HED; mg/kg basis; human therapeutic dose, 0.84 mg/area) was administered every other day for 16 days, 4/54 rat deaths due to dose-limiting signs at the injection site occurred. Injection-site perivasculard edema, hemorrhage, inflammation, fibrosis, and/or necrosis was seen. Partial/complete reversal of injection-site findings occurred during recovery. At CCH ≥0.13 mg (≥43× HED), the liver enzymes aspartate aminotransferase and alanine aminotransferase were elevated in male rats. At 96× HED, further liver findings (minimal/marked multifocal hemorrhage/hematoma, fibrosis, and/or hepatocellular necrosis) were noted and correlated to gross necropsy findings. Liver findings reversed partially at the 0.29 mg dose (96× HED) and mostly reversed at the 0.13 mg dose (43× HED). After IV administration in rats, plasma concentrations of AUX-I and AUX-II (Clostridial class I and II collagenases; 2 components of CCH) were measurable for 30 min and 1 to 2 h post-dose, respectively. For human subcutaneous PK studies, there were no quantifiable plasma concentrations of AUX-I and AUX-II at any time point post-dose for 28 evaluable women. Adverse events were injection site–related (bruising [96.6%], pain [82.8%], and edema [44.8%]). Antidrug antibodies were seen in 69.0% of 29 women at 504 h post-dose.

LIMITATIONS: Limitations included use of animal data to evaluate inadvertent IV dosing and that the human PK studies evaluated single-dose (session) subcutaneous administration only.

CONCLUSION: Repeat-dose IV administration (every other day; 8 dose administrations) at 43× HED dose in rats (on a mg/kg basis) was reasonably well tolerated. No quantifiable circulating CCH levels were observed in humans after a single subcutaneous dose of CCH up to 1.68 mg.

FUNDING: Endo Pharmaceuticals Inc.
Mean age was 48.1 years and mean weight was 90.8 kg; 70.3% of pts were male. Mean baseline PASI and BSA were 20.3 and 26.1%, respectively. A history of diagnosed or suspected PsA was reported in 30.9% of pts. Of the 1305 pts included in this integrated analyses, 19.7% were naïve to all treatment except topical therapy and 30.0% were naïve to systemic therapy. Prior psoriasis therapy included received phototherapy (31.2%), photochemotherapy (8.7%), non-biologic systemic therapy (47.8%), and biologic therapy (44.8%). TNFi therapy was reported in 28.1% of pts, while 29.6% received non-TNFi biologic therapy. A total of 218 pts reported failure of ≥1 prior biologic therapy; a majority was failure of at least one prior TNFi therapy. At wk 16, RZB-treated pts achieved significantly higher PASI 90 and sPGA 0/1 response rates compared with PBO-treated pts (P<0.001 for both endpoints across all subgroups), regardless of previous psoriasis treatment history. The efficacy of RZB in each of the subpopulations was comparable to the overall efficacy in the pooled population.

CONCLUSION: Treatment with RZB was associated with superior efficacy compared with PBO in adult pts with moderate-to-severe plaque psoriasis, regardless of previous psoriasis treatment history, including prior biologic failure.

DISCLOSURES: B Strober has received honoraria as a consultant from AbbVie, Almirall, Amgen, Astra Zeneca, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Janssen, Leo, Medac, Menlo Therapeutics, Novartis, Ortho Dermatologics/Valeant, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, and UCB Pharma; scientific director for the CORRONA-NPF Psoriasis Registry. J Lambert serves as an investigator and/or consultant for AbbVie, Celgene, Janssen, Lilly, Leo Pharma Novartis, Pfizer, and UCB. Y Gu, EHZ Thompson, and WC Valdecantos are full-time employees of AbbVie and may own stock/options. A Menter has received grants and honoraria from AbbVie, Amgen, Janssen Biotech, Inc., and LEO Pharma for service on an advisory board, as consultant, investigator, and speaker; received grants and honoraria from Allergan for service on an advisory board and as a consultant and from Eli Lilly for service on an advisory board, as a consultant and investigator; received grants and honoraria from Boehringr Ingelheim for service on an advisory board and as an investigator; received grants and honoraria from Novartis, and Pfizer for service as a consultant and investigator; received grants from Celgene, Dermira, Merck, Neothetics, Regeneron, and Syntrix for service as an investigator; and received honoraria from Galderma for service as a consultant.

ACKNOWLEDGMENTS: AbbVie and Boehringer Ingelheim funded the IMMhance (NCT02672852), UltIMMa-1 (NCT02684370), and UltIMMa-2 (NCT02684357) studies; Boehringer Ingelheim contributed to its design and participated in data collection, AbbVie performed the data analysis, and participated in interpretation of the data, and both participated in writing, review, and approval of the abstract. AbbVie, Boehringer Ingelheim, and the authors thank all study investigators for their contributions and the patients who participated in this study. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

PA-32: Indirect Comparison of Ixekizumab Versus Guselkumab Up to Week 12

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BACKGROUND: Biologics are effective for the treatment of psoriasis, but head-to-head studies comparing the efficacy of the recently approved biologics are lacking for certain comparators of interest.

OBJECTIVES: We indirectly compared psoriasis clinical trial efficacy data between ixekizumab (IXE), a selective interleukin (IL)-17A antagonist, and guselkumab (GUS), a recently approved IL-23 p19 inhibitor.

METHODS: We used the adjusted indirect comparison (AIC) Bucher method (BU) and two modified Signorovitch methods (SG) matching for overall or adjusting for baseline characteristics and effect modifiers to compare IXE 80 mg every 2 weeks (IXEQ2W) to GUS 100 mg (week 0, 4, 12) via the common comparator (bridge), placebo, with respect to Psoriasis Area Severity Index (PASI) response rates over the first 12 weeks.

RESULTS: Using the BU, PASI75 response rate at Week 2 for IXEQ2W was 20.0% higher than GUS (p<0.001) 95% CI: 17.3, 22.5. Response differences (RDs) for IXEQ2W vs GUS were 31.1% (95% CI: 25.0, 37.1) at Week 4 (p<0.001); 14.6% (95% CI: 8.3, 20.7) at Week 8 (p<0.001); and 8.3% (95% CI: 2.4, 14.1) at Week 12 (p=0.005). PASI90 RDs for IXEQ2W vs GUS were 21.7% (95% CI: 18.8, 24.5) at Week 4; 20.8% (95% CI: 18.8, 24.5) at Week 8; and 12.4% (95% CI: 6.0, 18.6) at Week 12 (all p<0.001). PASI100 RDs were 7.3% (95% CI: 5.7, 8.9) at Week 4; 15.6% (95% CI: 11.7, 19.5) at Week 8; and 16.4% (95% CI: 11.2, 21.6) at Week 12 (all p<0.001). With regard to PASI90 response rates differed significantly, favoring IXE over GUS at all time-points up to Week 12. The SG approaches were consistent with the BU results.

CONCLUSION: This indirect comparison indicates that IXE might provide clinical benefits over GUS in terms of onset of action and higher levels of skin clearance up to Week 12.

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FUNDING: This study was sponsored and funded by Eli Lilly and Company and INC Research.

PA-33: Interim Analysis of Phase 2 Results for Cemiplimab, a Human Monoclonal Antibody to Programmed Death-1, in Patients with Locally Advanced Cutaneous Squamous Cell Carcinoma (laCSCC)


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BACKGROUND: CSCC is the second most common skin cancer after basal cell carcinoma. There is no standard of care for patients with laCSCC (tumors without nodal or distant metastases not amenable to surgery or radiation). Cemiplimab (REGN2810) 3 mg/kg every 2 weeks (Q2W) demonstrated encouraging preliminary activity in advanced CSCC in a phase 1 study. We present an interim analysis of the laCSCC cohort from the pivotal phase 2 study (NCT02760498).

METHODS: Patients received cemiplimab 3 mg/kg Q2W intravenously over at least 30 minutes. Tumor measurements were performed Q8W. The primary objective was to evaluate overall response rate (ORR; complete response [CR] + partial response [PR]) by independent central review (per RECIST 1.1 for scans; modified WHO criteria for photos). Duration of response (DOR) was a key secondary endpoint.

Durable disease control rate (DDCR) was defined as stable disease or response for ≥16 weeks. This prespecified interim analysis includes patients who started study treatment ≥9 months prior to the data cut-off date (Oct 27, 2017).

RESULTS: 23 patients were eligible for this analysis (17 M/ 6 F; median age: 67.0 years [range: 47–96]). Six patients (26.1%) had received prior cancer-related systemic therapy; 14 (60.9%) had received prior radiotherapy. Median duration of follow-up was 9.7 months (range: 0.8–15.9). ORR by central review was 43.5% (95% CI: 23.2–65.5; 0 CRs and 10 PRs). DDCR was 69.6% (95% CI: 47.1–86.8). Median DOR has not been reached. The longest DOR at the time of data cut-off was 12.9+ months. Median time to response was 2.8 months (range: 1.9–7.6). The most common treatment-related adverse events (TRAEs) of any grade were fatigue (30.4%), nausea (21.7%), diarrhea (17.4%), and hypothyroidism (17.4%). The following ≥Grade 3 TRAEs were reported: dizziness (n=1) and increased aspartate aminotransferase (n=1). One patient developed hyponatremia and pneumonia that were assessed as unrelated to treatment and died due to unknown cause that was assessed as treatment-related.

CONCLUSIONS: In this prespecified interim analysis of patients with laCSCC, cemiplimab 3 mg/kg Q2W produced substantial activity and durable responses. The safety profile was comparable with other anti-programmed death-1 agents.

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FUNDING: Regeneron Pharmaceutical Inc. and Sanofi

DISCLOSURES: Michael R. Migden: reports honoraria/travel expenses from Regeneron Pharmaceuticals, Inc., Novartis, Genentech, Eli Lilly, and Sun Pharma; and institutional research funding from Regeneron Pharmaceuticals, Inc., Novartis, Genentech, and Eli Lilly. Carola Berking: reports institutional grants, consultancy fees and/or speaker’s honoraria from Amgen, AstraZeneca, Bristol-Myers Squibb, MSD, Novartis, and Roche; consultancy fees and/or speaker’s honoraria from Incyte, Merck, Pierre Fabre, and Sanofi-Aventis; and institutional grants from Array Pharma and Regeneron Pharmaceuticals, Inc. Anne Lynn S. Chang: reports grant from Regeneron Pharmaceuticals, Inc., during the conduct of the study. Thomas K. Eigentler: reports institutional grants, consultancy fees and/or speaker’s honoraria from Amgen, AstraZeneca, Bristol-Myers Squibb, MSD, Novartis, and Roche; consultancy fees and/or speaker’s honoraria from Amgen, AstraZeneca, Bristol-Myers Squibb, MSD, Novartis, and Roche; institutional grants and consultancy fees from Merck Sharp Dohme, outside the submitted work. Axel Hauschild: reports institutional grants, speaker’s honoraria and consultancy fees from Amgen, Bristol-Myers Squibb, MSD/Merck, Pierre Fabre, Proveuctus, Roche, and Novartis; institutional grants and consultancy fees from Merck Serono, Philogen, and Regeneron Pharmaceuticals, Inc.; and consultancy fees from OncoSec. Leonel Hernandez-Aya: reports institutional
fees from Regeneron Pharmaceuticals, Inc. during the conduct of the study; institutional fees from BMS, Merck, Amgen, Roche, Novartis, Immunocore, Merck-EMD, Corvus, Polynoma, and Genentech. Nikhil I. Khushalani: reports grant from Regeneron Pharmaceuticals, Inc. during the conduct of the study; grants and advisory board fees from Bristol-Myers Squibb and HUYA Bioscience International; advisory board fees from EMD Serono, Regeneron Pharmaceuticals, Inc., Genentech, and Astra Zeneca (Data safety monitoring committee); grants from Merck, Novartis, GlaxoSmithKline, and Amgen; and common stock ownership from Bellicum Pharmaceuticals and Mazor Robotics, outside the submitted work. Karl D. Lewis: reports grant and consulting fees from Regeneron Pharmaceuticals, Inc. during the conduct of the study. Friedegund Meier: reports fees for clinical study from Regeneron Pharmaceuticals, Inc. during the conduct of the study. Badri Modi: declares no conflict of interest. Danny Rischin: reports institutional clinical trial funding from Regeneron Pharmaceuticals, Inc., during the conduct of the study; institutional clinical trial funding and grants from Roche Genentech and GSK; institutional clinical trial funding and uncompensated scientific committee and advisory board from Merck (MSD), Bristol-Myers Squibb, and Amgen and institutional clinical trial funding from Threshold Pharmaceuticals. Dirk Schadendorf: reports institutional patients’ fees from Regeneron Pharmaceuticals, Inc., during the conduct of the study; adboard honorarium fees from Amgen and Leo Pharma; speaker fee from Boehringer Ingelheim; adboard, speaker honorarium, and patients’ fees from Roche, Novartis, BMS, and Merck-EMD; adboard and speaker honorarium fees from Incyte and Pierre Fabre; adboard honorarium and patients’ fees from MSD, steering cei honorarium fees from 4SC, adboard fees from AstraZeneca, Pfizer, and Array; and adboard and patients’ fees from Philogen. Chrysalyne D. Schmults: reports participating as steering committee member with Castle Biosciences, grants (basal cell staging) from Genentech, grants (cutaneous squamous cell carcinoma [Investigational programmed cell death-1 drug]) from Regeneron Pharmaceuticals, Inc., outside the submitted work. Claas Ulrich: reports grant from Regeneron Pharmaceuticals, Inc., during the conduct of the study. Jocelyn Booth: is an employee of Regeneron Pharmaceuticals, Inc. Siyu Li: is an employee of Regeneron Pharmaceuticals, Inc. Kosalai Mohan: is an employee of Regeneron Pharmaceuticals, Inc. Elizabeth Stankevich: is an employee and shareholder of and has received accommodation and travel expenses from Regeneron Pharmaceuticals, Inc. Israel Lowy: is an employee, has been compensated for leadership roles, is a shareholder of and has received fees for accommodation and travel expenses from Regeneron Pharmaceuticals, Inc. Matthew G. Fury: is an employee and shareholder of and has received fees for patents, royalties, or other intellectual property and accommodation and travel expenses from Regeneron Pharmaceuticals, Inc.

**PA-34: Isotretinoin, Creatine Kinase, and Physical Activity: A Pilot Study**

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**BACKGROUND:** Oral isotretinoin (OI) is a prescribed therapy for severe, nodulocystic acne vulgaris or recalcitrant acne unresponsive to topical and antibiotic therapy. Since its US debut in 1982, OI has been reported to cause elevations in a marker for muscle tissue damage, creatine kinase (CK). Elevation of serum CK levels usually correlates with damage to tissue or intrinsic muscle pathology that results in disruption of the cellular membranes and leakage of CK into systemic circulation, with potential to cause rhabdomyolysis (CK greater than five times the reference range), kidney failure, and even death.

**CONFLICTS:** None.

**OBJECTIVES:** To determine correlation between observed CK elevations in patients on OI therapy and patient’s demographic information including age, gender, activity status, and OI dosage by reviewing and analyzing patient records.

**METHODS:** We used data from patients who were active on our physician IPledge registry (N=46). We excluded patients that did not have their serum CK evaluated during therapy (N=22), patients that had aspartate aminotransferase (AST) or alanine aminotransferase (ALT) drawn in lieu of CK (N=3), and patients that had not had at least two separate CK evaluations while on OI therapy (N=5). In total 15 patients were part of the final analysis (Male, N=10; Female, N=5). Data collected from the chart review included age, sex, serum CK values during prior to and during therapy, prescribed dosage of OI, length of OI therapy, physical activity including self-reported weightlifting, long-distance running, or more than one high-intensity varsity sport (ie football, soccer, hockey, lacrosse, etc.) and review of systems. Analysis was performed using R. P-values were calculated based on t-test for pairwise comparisons, paired t-test for longitudinal analysis of individual serum CK values, or fisher’s exact test for categories comparisons.

**RESULTS:** Between females who reported physical activity and those who did not, we found a significant difference in accumulated dose of OI therapy prior to their highest serum CK value (13.2 mg/Kg vs 39.3 mg/Kg; p=0.030), weeks of OI therapy prior to serum CK elevation (4 weeks vs 10.6 weeks, p=0.030) and baseline CK (108 IU/L vs 68 IU/L, p=0.013). Of these patients, only 1 female (who also reported physical activity) had a maximum serum CK above 100 IU/L while only 1 male (who reported no physical activity)
had a maximum serum CK below 100 IU/L (p=0.017). Only two patients had maximum serum CK values that approached 1000 IU/L (998 IU/L and 4,269 IU/L). Both of these patients were males who reported significant strenuous physical activity (weightlifting and firefighting, and long-distance running, respectively); however, neither reported physical symptoms at any point during therapy. Furthermore, no patient on our active registry has reported any physical symptom while on OI therapy.

LIMITATIONS: Analysis of our chart review was limited primarily by small sample size (N=15). Because our patient population came predominately from Morristown, NJ, and Brooklyn, NY, results may not be representative of the entire patient population on OI therapy. Furthermore, several patients were either unable to or did not have their lab results evaluated on a monthly basis leading to incomplete data for analysis.

CONCLUSION: The current body of evidence supports a tenuous correlation between OI and elevated serum CK, especially with concurrent physical activity. Our preliminary chart review found that females who reported physical activity reached their respective maximum serum CK value in less time and with a lower cumulative dose of OI than their non-active female counterparts. Our preliminary results found no difference between serum CK values between males and females and could not analyze differences between physically active and non-active males. These initial results, although they did not reach significance, are consistent with the current body of knowledge intimating that males have higher CK values than females, and because physically active males have the potential to have the highest values and the greatest risk of developing rhabdomyolysis, they may require regular laboratory monitoring. Further studies are required to disentangle the extent to which OI therapy and physical activity elevate serum CK, and other factors inherent to the patient and to OI dosage that may predispose patients to serum CK elevation and muscle symptoms during OI therapy.

PA-35: IVlg Drug Induced Lupus in CIDP Patients

BACKGROUND: Drug induced lupus is well recognized by dermatologists. Myriad drugs have been associated with drug induced SLE and drug induced cutaneous lupus. Each drug often has a typical presentation associated. IVlg is not well represented in those medications in the dermatology literature. There appears to be a rare subset of patients with CIDP treated with IVlg who appear to be at increased risk of developing a drug induced lupus that is characterized by cutaneous lesions and anti-Ro, -La.

OBJECTIVE: We seek to bring this subset of patients to wider recognition in hopes of stimulating investigation into this peculiar occurrence and whether it applies to IVlg broadly, or only to this particular disease.

METHODS: Single case presented with histology, laboratory data, clinical photos, along with literature review of similar cases.

LIMITATIONS: This is a single case with gross and microscopic presentation and a review of a handful of similar cases found in publications without wide readership.

CONCLUSIONS: There appears to be an elevated risk of developing a drug induced lupus state characterized by anti-Ro, -La, and in this case, -Histone antibodies, in patients with CIDP who receive IVlg. This requires further study to determine whether it is peculiar to CIDP patients receiving IVlg, or whether this may apply to IVlg in general as it is not widely recognized in dermatology as a cause of systemic or cutaneous lupus.

ABSTRACT: A 27 y.o. Caucasian male with a long standing diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) on IVlg therapy who developed chronic cutaneous lupus. An extensive autoimmune workup and consultations during initial encounters 4 years prior revealed no signs of systemic or cutaneous lupus. He was started on and failed multiple immunosuppressive medications, eventually requiring long term IVlg and mycophenolate therapies. Four years after initiation of IVlg, the patient presented with classic discoid lupus lesions in a photodistribution, and biopsy was consistent. Rheumatology consultation was not consistent with systemic lupus. Though he met >4 of 11 ACR criteria, he could not fulfill the SLICC criteria. Laboratory evaluation the second time revealed mild pancytopenia along with elevated ANA, Ro, La, anti- histone antibodies and sedimentation rate. Anti-dsDNA antibodies, complement levels, and myositis panels were notably negative. This may indicate CIDP patients are at risk of developing a drug induced cutaneous lupus syndrome that is peculiar in that it appears to have higher likelihood of cutaneous involvement, and positive Ro/La antibodies than is classically attributed to drug induced lupus. This type of drug induced lupus appears not to be well recognized or reported in the dermatology literature to this point, and appears to only be reported in patients with CIDP thus far. As IVlg is not infrequently used by dermatologists, this question requires more investigation to determine whether there is a true risk of developing lupus after IVlg administration.

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DISCLOSURES: The author has no financial interests or conflicts of interest to disclose.

PA-36: Ixekizumab Provides Sustained Improvement in Signs and Symptoms in Patients with Active Psoriatic Arthritis: Two-Year Results from a Phase 3 Trial

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BACKGROUND: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets IL-17A. In the SPIRIT-P1 phase 3 study (NCT01695239), IXE was superior to placebo (PBO) in achieving ACR20 response at Week 24 in biologic DMARD (bDMARD)-naive patients with active psoriatic arthritis (PsA).

OBJECTIVES: Here, the efficacy and safety of IXE over 2 years in SPIRIT-P1 is evaluated.

METHODS: During the SPIRIT-P1 double-blind treatment period (DBTP; Weeks 0-24), 417 bDMARD-naive patients with active PsA were randomized 1:1:1:1 to 80 mg subcutaneous IXE (160 mg starting dose at Week 0) every 4 weeks (Q4W), every 2 weeks (Q2W), 40 mg adalimumab every 2 weeks (ADA, active reference arm), or PBO. Of these, 381 patients entered the extension period (Weeks 24-52), followed by the long-term extension period (Weeks 52-156). Data presented here are for the combined CEP population: an ADA/IXE Q4W patient with a history of dyslipidemia, diabetes mellitus, hypertension, and a previous transient ischemic attack, suffered a cerebrovascular accident at Week 108.

RESULTS: Serious AEs occurred in 46 patients. One death occurred in the IXE arm and the majority were mild or moderate in severity; 9 transient ischemic attacks were observed at Week 108. Frequency of treatment-emergent adverse events (AEs) were similar across treatment arms and the majority were mild or moderate in severity; serious AEs occurred in 46 patients. One death occurred in the CEP population: an ADA/IXE Q4W patient with a history of dyslipidemia, diabetes mellitus, hypertension, and a previous transient ischemic attack, suffered a cerebrovascular accident at Week 108.

CONCLUSION: For patients naïve to biologic treatment, IXE demonstrated clinically significant improvement in the signs and symptoms of PsA across treatment groups up to 2 years of treatment. The safety profile of IXE observed during the CEP was similar to that observed in the DBTP of SPIRIT-P1 and SPIRIT-P2, as well as other phase 3 studies of IXE in patients with plaque psoriasis.

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PA-37: Lipofilling of Tissue Deficits: Does N-Acetylcysteine Improve Graft Survivability?

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BACKGROUND: Tissue deficits, resulting from disease, aging, and trauma, remain a problem of cosmetic and psychological matter. Slight imperfections can be maintained with dermal fillers, but larger defects need adequate volume restoration by implants or translocated autologous tissues. Lipofilling is perceived as an optimal treatment method of medium tissue deficits, due to easy harvesting procedure, biocompatibility, and natural final effect. However, the unpredictability of long-term fat graft survival hinders proper graft input.

OBJECTIVES: This first-in-human pilot study aimed to determine if N-acetylcysteine (NAC) delivered at the fat graft donor site during the harvest procedure reduces oxidative stress and therefore, enhances graft survivability. The study was registered on ClinicalTrials.gov. Trial registry name: The Impact of N-Acetylcysteine on Volumetric Retention of Autologous Fat Graft for Breast Asymmetry Correction. Registration identification number: NCT03197103

METHODS: 15 women with breast asymmetry were included in the study (mean age of 31.8 years, range: 23–39 years). Every study subject underwent 200-ml adipose tissue graft harvesting procedure, separately from each thigh. The protocol of graft harvesting in the control thigh (n=15), included infiltration with a standard Klein tumescent fluid. During the graft harvesting from the contralateral thigh (NAC group, n=15), a tumescent fluid was enriched with NAC (Sandoz, Holzkirchen, Germany). A board-certified plastic surgeon, who performed the procedure, has been blinded to the type of administered fluid. After the surgery, 6-months follow-up was maintained. 65-ml aliquote of adipose tissue from each graft were analyzed via: Real-Time Polymerase Chain Reaction (RT-PCR), flow cytometric

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assay, biochemical analyses (on fresh and frozen samples). Remaining graft volumes were used for the correction of breast asymmetry (analysis of fat resorption by comparison of pre- and postoperative MRI scans in separate study). During biochemical tests, the severity of oxidative stress was determined based on the levels of reactive oxygen species (ROS) and nitric oxide (NO), along with the concentration and activity of superoxide dismutase (SOD). qRT-PCR analysis included targets reflecting oxidative stress (GPX-3, hsCAT, hsSOD, iNOS, HO-1), angiogenesis (VEGF, ANG-2, and adipogenesis (PPAR-γ, C/EBPγ). Normal distribution of the data was confirmed with the Kolmogorov-Smirnov test. Intragroup comparisons were carried out with Wilcoxon signed-rank test.

RESULTS: During follow-up, no postoperative complications has been observed. The concentration of SOD in the NAC group was significantly higher than in the controls, in both fresh and frozen samples (p=0.041 and p=0.004, respectively). However, ROS particles level analysis revealed no statistically significant intergroup differences. The NO level in frozen samples from the controls was significantly higher than in NAC group (p<0.01), which was also followed by increased iNOS (inducible NO synthase) expression in qRT-PCR assay in the controls (p=0.027). Remaining mRNA targets showed no significant up- or downregulation in NAC group vs controls (p>0.05). Flow cytometry analysis of live/dead cells showed no significant differences between groups as well as live cells’ yield (p>0.05).

CONCLUSIONS: The results of this study suggest that the enrichment of NAC in the tumescent solution may decrease the consequences of oxidative stress exposure to the cells of the autologous fat graft during the harvesting procedure. In turn, it may decrease resorption of the fat graft in a recipient site over time (the MRI study is still ongoing). If the addition of NAC was shown to improve the retention of the graft, this technique might become a standard and safe method of fat harvesting for filling purposes. Further studies may prove the use of NAC as protective agent in adipose tissue biobanking.

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DISCLOSURES: All authors have nothing to disclose.

FUNDING: This study was partially supported by a statutory research activity grant received from Centre of Postgraduate Medical Education in Warsaw (501-1-06-09-17).

PA-38: Long-Term Management of Moderate-to-Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Fixed Combination Halobetasol Propionate 0.01% and Tazarotene 0.045% (HP/TAZ) Lotion

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DISCLOSURES: PSY and JSS are advisors to Ortho Dermatologics and investigators with Dow Pharmaceutical Sciences. TL and RP are employees of Bausch Health

BACKGROUND: Psoriasis is an immune-mediated disease; often chronic with frequent remissions and exacerbations. Patients often stop treatment, restart, or switch therapy. Adherence to topical therapy is generally poor in the majority of the patients, although seen to improve with simple regimens and once-a-day therapy. Data on maintenance of efficacy posttreatment are sparse.

OBJECTIVE: To evaluate the maintenance of treatment success following cessation of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) lotion in moderate-to-severe psoriasis.

METHODS: One-year multicenter, open-label study in 555 subjects (mean age 51.9 years) with moderate-to-severe plaque psoriasis treated with HP/TAZ lotion. Patients were treated with HP/TAZ lotion once-daily for 8 weeks and then as needed; treatment success defined as an Investigator Global Assessment (IGA) score of 0 or 1 (“Clear” or “Almost Clear”).

Patients who did not reach treatment success at Week 8 were treated for a further 4 weeks; otherwise they received no further treatment at this time. All patients were evaluated at Week 12; those demonstrating 1-grade improvement in baseline IGA were subsequently maintained in four-week cycles; either treated with HP/TAZ lotion once-daily if they had not achieved treatment success or receiving no treatment until the next evaluation if they had achieved treatment success, with a maximum continuous exposure of 24 weeks.

RESULTS: Overall, 318 patients (57.3%) achieved treatment success at some point during the study; the majority (54.4%, N=173) within the first 8 weeks. In many, treatment success was more rapid, being achieved within the first 2 and 4 weeks in 12.6% and 37.4% of patients, respectively. Of those patients who stopped therapy after achieving treatment success, 6.6% (N=15) did not require any retreatment, 28.3% did not require retreatment for at least 2 months, and the majority (55.3%) did not require retreatment for at least one month. These data are consistent with those reported in the earlier studies with HP/TAZ lotion where 55% of patients who were treatment successes remained so at the end of the 4-week posttreatment follow-up.

LIMITATIONS: This was an open-label study.

CONCLUSIONS: HP/TAZ lotion provides rapid and sustained treatment success in patients with moderate-to-severe psoriasis when followed for 1 year.
PA-39: Long-Term Efficacy and Safety of Brodalumab by Prior Psoriasis Treatment Status

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BACKGROUND: Brodalumab is a fully human anti–interleukin-17 receptor monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis in adults.

OBJECTIVE: To assess the long-term efficacy and safety of brodalumab in patients with moderate-to-severe plaque psoriasis stratified by categories of prior psoriasis treatments using a post-hoc analysis of 2 multicenter randomized clinical trials (AMAGINE-2/3).

METHODS: Patients were initially randomized to brodalumab every 2 weeks, ustekinumab, or placebo. At week 52, all patients entered the long-term extension and received brodalumab. Skin clearance was assessed by 75% improvement in psoriasis area and severity index from baseline (PASI 75) and PASI 100. Efficacy data were reported through 120 weeks using observed data, last observation carried forward (LOCF), and non-responder imputation (NRI) analyses for patients who received any dose of brodalumab. Safety was summarized by exposure-adjusted rates of treatment-emergent adverse events (TEAEs).

RESULTS: Among 3625 patients in the efficacy analysis at baseline, previous psoriasis treatments were reported using the following non–mutually exclusive categories: systemic or phototherapy (n=2636), methotrexate (n=976), acitretin (n=475), cyclosporine (n=385), and steroids (n=161). At week 52, across all subgroups, 87.4% to 92.7% of brodalumab-treated patients achieved PASI 75 and 44.1% to 59.9% achieved PASI 100. PASI 75 responses by previous psoriasis treatment category (systemic or phototherapy, methotrexate, acitretin, cyclosporine, and steroids) at week 120 using observed data analysis were 88.7%, 87.4%, 89.7%, 90.2%, and 84.8%, respectively; PASI 100 responses at week 120 were 57.2%, 56.4%, 60.1%, 63.7%, and 45.6%, respectively. At week 120, PASI 100 responses by previous psoriasis treatment category (systemic or phototherapy, methotrexate, acitretin, cyclosporine, and steroids) using LOCF analysis were 47.0%, 46.3%, 50.9%, 52.5%, and 43.1%, respectively; PASI 100 responses at week 120 using NRI analysis were 29.6%, 29.3%, 30.7%, 35.6%, and 22.4%, respectively. In the 12-week induction phase, exposure-adjusted TEAE rates in those treated with brodalumab ranged from 614.8 to 745.6 per 100 patient-years across previous psoriasis treatment categories; exposure-adjusted TEAE rates with placebo ranged from 399.4 to 616.1 per 100 patient-years. Over all study years, exposure-adjusted TEAE rates with brodalumab were 276.5 to 318.2 per 100 patient-years.

CONCLUSIONS: Skin clearance efficacy was maintained at high rates through 120 weeks among patients with moderate-to-severe psoriasis who received brodalumab regardless of previous exposure to psoriasis treatments. Brodalumab was efficacious and well tolerated in patients with prior exposure to psoriasis therapies.

FUNDING: This study was sponsored by Ortho Dermatologics. Medical writing support was provided by MedThink SciCom under the direction of the authors and was funded by Ortho Dermatologics.

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DISCLOSURES: Craig Leonardi has served as a consultant to or an advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Pfizer, Sandoz, UCB, and Vitae; has served as an investigator for Actavis, AbbVie, Allergan, Amgen, Boehringer Ingelheim, Celgene, Coherus, Cellectux, Corrona, Dermira, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck, Novartis, Novella, Pfizer, Sandoz, Sienna, Stiefel, UCB, and Wyeth; and has participated in speakers bureaus for AbbVie, Celgene, Novartis, Sun Pharma, and Eli Lilly. Alice Gottlieb has served as a consultant to or an advisory board member for Janssen, Celgene, Bristol-Myers Squibb, Beiersdorf, AbbVie, UCB, Novartis, Incyte, Eli Lilly, Dr Reddy’s Laboratories, Bausch Health, Dermira, Allergan, and Sun Pharma and has received research or educational grants from Incyte and Janssen. Jennifer Soung has received compensation from or served as an investigator, consultant, advisory board member, or speaker for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Menlo, Merck, Novan, Novartis, Pfizer, Roche, Regeneron, Sun Pharma, Sanofi Genzyme, Cassiopeia, UCB, and Valeant.

PA-40: Long-Term Efficacy and Safety of Ixekizumab for the Treatment of Moderate-to-Severe Plaque Psoriasis Sustained for 3 Years: Results of a Randomized, Controlled Phase 3 Study (UNCOVER-3)

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BACKGROUND: Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A, has been indicated for treating patients with moderate-to-severe...

**OBJECTIVE:** We report the efficacy of 3 years (156 weeks) of treatment with IXE from UNCOVER-3 study.

**METHODS:** A total of 1346 patients were randomized (2:2:2:1) to treatment groups receiving sc IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) following an initial dose of IXE 160 mg, etanercept 50 mg twice weekly, or placebo during the 12-week induction period. Patients entered the long-term extension (LTE) period with IXE Q4W dosing at Week 12. Dosing could be adjusted to IXE Q2W at investigator’s discretion after Week 60. Efficacy data were considered for analysis only when patients were treated with recommended IXE dose (n=385), that is, the data collected at visits with adjusted Q2W were excluded before imputations were applied. The efficacy was measured by percentage of patients who achieved a 75%, 90%, or 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI) and a static Physician’s Global Assessment (sPGA) score of 0/1 or 0. Efficacy data were summarized for the intent-to-treat population for 3 years using as-observed, multiple imputation (MI), and a modified non-responder imputation (mNRI) approach for missing data.

**RESULTS:** Of 1346 randomized patients, 1037 (77.0%) completed 3 years of efficacy assessment. IXE sustained high skin clearance rates throughout 3 years of treatment, measured by PASI 75/90/100 and sPGA 0/1 or 0. With IXE Q2W/IXE Q4W recommended dose, the proportion of patients who achieved the efficacy (as-observed, MI, mNRI, respectively) was PASI 75: 97%, 86%, 81%; PASI 90: 87%, 70%, 66%; and PASI 100: 64%, 47%, 45%; sPGA 0/1: 85%, 73%, 67%; and sPGA 0: 64%, 52%, 49%. Of 1274 patients who entered LTE, 182 (14.3%) had a dose adjustment to IXE Q2W between Week 60 and Year 3. Infections remained the most commonly observed adverse events, and the majority of treatment-emergent adverse events during the extension period continued to be mild or moderate in severity.

**CONCLUSIONS:** This study demonstrated that high efficacy response with ixekizumab treatment was sustained over 3 years in patients with moderate-to-severe plaque psoriasis. The safety profile was consistent with prior findings without any new safety concerns.

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**PA-41: Long-Term Efficacy, Safety, and Patient-Reported Outcomes in a Phase 2 Study of Brodalumab**

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**BACKGROUND:** Brodalumab is a fully human anti– interleukin-17 receptor A monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis. Brodalumab demonstrated rapid and robust levels of skin clearance in a 12-week, double-blinded, phase 2 study in patients with psoriasis.

**OBJECTIVES:** This analysis evaluated the long-term efficacy and safety of brodalumab in an open-label extension (OLE) of the phase 2 study.

**METHODS:** In the parent study, patients were randomized to brodalumab (70, 140, 210, or 280 mg) or placebo for 12 weeks. All patients in the OLE initially received brodalumab 210 mg every 2 weeks (Q2W); dose reduction to 140 mg Q2W was later allowed in patients weighing ≤100 kg, along with a subsequent dose increase to 210 mg Q2W in patients with an inadequate response to 140 mg Q2W. Efficacy was assessed by psoriasis area severity index (PASI) ≥75% improvement response (PASI 75) and PASI 100 (observed data analysis). Safety was reviewed in all patients who received ≥1 dose of brodalumab using the incidence of treatment-emergent adverse events (TEAEs) and serious AEs. Other assessments included the percentage of patients with a dermatology life quality index (DLQI) score of 0 or 1. Efficacy data were analyzed at weeks 12, 48, 96, 168, 216, and 264.

**RESULTS:** A total of 181 patients (117 men and 64 women; mean [standard deviation] age 42.7 [12.2] years; 90% white) entered the OLE; 107 patients remained on treatment at week 264. There were 118 patients (65%) who had a dose reduction from brodalumab 210 to 140 mg owing to body weight ≤100 kg, and 30 patients (17%) had a dose increase to 210 mg because of an inadequate response. Median (interquartile range) duration of brodalumab exposure was 264 (200-274) weeks. Efficacy with brodalumab was maintained from week 12 up to week 264, with PASI 75 responses consistently ≥80% and PASI 100 responses ≥40%. There was a decrease in response across all treatment groups at week 264 (final study visit), when patients had been off treatment for ≥6 weeks. The percentage of patients with DLQI score of 0 or 1 was 84% at week 12 and 68% at week 264. A greater percentage of patients with PASI 100 responses had a DLQI score of 0 or 1 at week 264 (96% [n/N=27/28]) than those with PASI 90 to <100 responses (86% [6/7]) or PASI 75 to <90 responses (40% [2/5]). Over all study years, TEAEs occurred in 177 patients; grade ≥3 TEAEs occurred in 41 patients (23%), and 29 patients (16%) had ≥1 serious AE. The most common TEAEs included nasopharyngitis, upper respiratory tract infection, and arthralgia (29%, 24%, and 20% of patients, respectively). No new safety signals emerged in the OLE period.

**CONCLUSIONS:** Brodalumab demonstrated high levels of skin clearance efficacy, improved dermatology quality of life, and was well tolerated through ~5 years of long-term treatment. Complete skin clearance (PASI 100) with brodalumab
was associated with improved quality of life relative to high levels of efficacy without total clearance (PASI 75 to <100).

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**DISCLOSURES:** Mark Lebwohl is an employee of Mount Sinai, which receives research funds from AbbVie, Boehringer Ingelheim, Bausch Health, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, Leo, Medimmune/AstraZeneca, Novartis, Pfizer, Sciderm, UCB, and Vicap, and is also a consultant for Allergan, Aqua, Arcutis, Boehringer Ingelheim, LEO Pharma, Menlo, and Promius. Andrew Blauvelt has served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, Bausch Health, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Meiji, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB, and Vicap and as a paid speaker for Janssen, Regeneron, and Sanofi Genzyme. Alan Menter has received compensation from or served as an investigator, consultant, advisory board member, or speaker for AbbVie, Allergan, Amgen, Anacor, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, Janssen Biotech, Leo, Merck & Co, Neothetics, Novartis, Pfizer, Regeneron, Symbio/Maruhou, Vitae, and Xenoprot. Kim Papp has served as a consultant, scientific officer, member of a speaker’s bureau, advisory board, or steering committee for or received research grants or honoraria from AbbVie, Akesis, Akros, Allergan, Alza, Amgen, Anacor, Artax Biopharma, Astellas, AstraZeneca, Bausch Health, Baxter, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite BioPharma, Celgene, Celtic Pharma, Cipher, Dermira, Dow Pharma, Eli Lilly, Ferring, Formycon, Forward Pharma, Fujisawa, Funxional Therapeutics, Galderma, Genentech, Genexon, Genzyme, Gilead, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin Co, Leo, Medimmune, Meiji Seika Pharma Co, Merck & Co (MSD), Merck Serono, Mitsubishi Tanabe Pharma, Mylan, Novartis, Novimmune, Pan-Genetics, Pfizer, Regeneron, Roche, Sanofi-Aventis, Stiefel Laboratories, Takeda, UCB, and Vertex Pharmaceuticals. Abby Jacobson is an employee of Ortho Dermatologics and holds stocks and/or stock options in Bausch Health.

**FUNDING:** This study was sponsored by Ortho Dermatologics. Medical writing support was provided by MedThink SciCom under the direction of the authors and was funded by Ortho Dermatologics.

**PA-42: Long-Term Management of Moderate-to-Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Fixed Combination Halobetasol Propionate 0.01% and Tazarotene 0.045% (HP/TAZ) Lotion.**

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**DISCLOSURES:** PSY and JSS are advisors to Ortho Dermatologics and investigators with Dow Pharmaceutical Sciences. TL and RP are employees of Bausch Health.

**BACKGROUND:** Psoriasis is an immune-mediated disease, often chronic with frequent remissions and exacerbations. Patients often stop treatment, restart, or switch therapy. Adherence to topical therapy is generally poor in the majority of the patients, although seen to improve with simple regimens and once-a-day therapy. Data on maintenance of efficacy post-treatment are sparse.

**OBJECTIVE:** To evaluate the maintenance of treatment success following cessation of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) lotion in moderate-to-severe psoriasis.

**METHODS:** One-year multicenter, open-label study in 555 subjects (mean age 51.9 years) with moderate-to-severe plaque psoriasis treated with HP/TAZ lotion. Patients were treated with HP/TAZ lotion once-daily for 8 weeks and then as needed; treatment success defined as an Investigator Global Assessment (IGA) score of 0 or 1 (“Clear” or “Almost Clear”).

Patients who did not reach treatment success at Week 8 were treated for a further 4 weeks; otherwise they received no further treatment at this time. All patients were evaluated at Week 12; those demonstrating 1-grade improvement in baseline IGA were subsequently managed in 4-week cycles; either treated with HP/TAZ lotion once-daily if they had not achieved treatment success or receiving no treatment until the next evaluation if they had achieved treatment success, with a maximum continuous exposure of 24 weeks.

**RESULTS:** Overall, 318 patients (57.3%) achieved treatment success at some point during the study; the majority (54.4%, N=173) within the first 8 weeks. In many, treatment success was more rapid, being achieved within the first 2 and 4 weeks in 12.6% and 37.4% of patients, respectively. Of those patients who stopped therapy after achieving treatment success, 6.6% (N=15) did not require any retreatment, 28.3% did not require retreatment for at least 2 months, and the majority (55.3%) did not require retreatment for at least one month. These data are consistent with those reported in the earlier studies with HP/TAZ lotion where 55% of patients who were treatment successes remained so at the end of the 4-week post-treatment follow-up.

**LIMITATIONS:** This was an open-label study.

**CONCLUSIONS:** HP/TAZ lotion provides rapid and sustained treatment success in patients with moderate-to-severe psoriasis when followed for 1 year.
**PA-43: Long-Term Safety and Efficacy of Adalimumab from the Phase 3 Randomized, Placebo-Controlled Trial in Patients with Nail and Skin Psoriasis**

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**INTRODUCTION:** We evaluated long-term (up to 52 weeks) safety and efficacy of originator adalimumab every-other-week treatment (ADA eow) for fingernail psoriasis (Ps) in patients (pts) with moderate-to-severe Ps with substantial, clinically impactful, moderate-to-severe fingernail Ps.

**METHODS:** In 26-week Period A, pts were randomized 1:1 to 40 mg ADA after initial 80 mg dose, or matching placebo (pbo). Period B (open-label, 26 weeks) entry criteria: completion of Period A, or ≥25% increase from baseline in affected body surface area (BSA) at week 16. At Period B entry (week 26), Period-A pbo pts received an initial blinded dose of 80 mg ADA; all received ADA eow from weeks 27 through 51. We analyzed all pts who received ADA throughout the 52 weeks. Efficacy is reported using multiple imputation (MI) for missing data, and as observed results.

**RESULTS:** Of the 217 randomized pts, 203 received at ≥1 dose of ADA, 188 entered Period B, and 168 completed the trial. Of those receiving continuing ADA treatment through 52 weeks (N=109), response rates (MI) for key efficacy outcomes at weeks 26 and 52, respectively, were as follows: ≥75% improvement from baseline in modified Nail Ps Severity Index (mNAPSI 75): 47.4% and 55.6%. Physician’s Global Assessment of fingernail Ps of 0 (clear) or 1 (minimal) with ≥2 grades improvement from baseline (PGA-F 0/1): 51.1% and 55.6%. Mean change (improvement) from baseline in nail Ps pain (numerical rating scale [NRS]): 3.6 and 3.8. Mean change (improvement) from baseline in NPPFS: 3.4 and 3.9. Mean change (improvement) from baseline in Dermatology Life Quality Index score (DLQI): 9.1 and 9.0 (N=94). As observed response rates at weeks 26 and 52, respectively, were as follows: mNAPSI 75: 47/88 (53.4%) and 52/80 (65.0%); PGA-F 0/1: 48/88 (54.5%) and 49/80 (61.3%). Mean change (improvement) from baseline in nail Ps pain (NRS): 3.8 (N=92) and 4.4 (N=80). Mean change (improvement) from baseline in NPPFS: 3.9 (N=92) and 4.4 (N=80). Mean change (improvement) from baseline in DLQI: 9.3 (N=69) and 9.7 (N=65). Adverse events (AEs) per 100 pt years (E/100PYs; in 140.3 PYs) were: any event, 352 (250.9), serious AEs, 21 (15.0), and serious infections, 9 (6.4). AEs were similar to those observed as observed results.

**CONCLUSION:** ADA treatment of nail Ps across 52 weeks demonstrated short- and long-term efficacy. No new safety signals were identified in these pts receiving ≥1 dose of ADA.

**DISCLOSURES:** Jeff Crowley received honoraria for consultant and speaker services from AbbVie, Amgen, Celgene, and Novartis, and grants for investigator services from AbbVie, Amgen, Astra-Zeneca, Boehringer Ingelheim, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, and Sandoz. Paolo Gisondi received honoraria for advisory board membership and/or speaker services from Abbvie, Novartis, Pfizer, Celgene, Eli Lilly, Sanofi, MSD, and Janssen. Z Geng receives a salary as an AbbVie employee, and may also receive stocks and/or stock options. O Reyes Servin receives a salary as an AbbVie employee, and may also receive stocks and/or stock options.

**ACKNOWLEDGMENTS:** AbbVie Inc. funded this study and participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing, and approving of this publication. All authors had access to the data, and participated in the development, review, and approval, and in the decision to submit this publication. The authors would like to acknowledge Jody Bennett, employed by AbbVie, for medical writing support in the production of this publication.

**PA-44: Malignancy Rates in the Brodalumab Psoriasis Clinical Studies**

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**BACKGROUND:** Brodalumab is a fully human anti–interleukin-17 receptor A (IL-17RA) monoclonal antibody that antagonizes cytokines involved in psoriasis pathogenesis and is efficacious in treating moderate-to-severe plaque psoriasis. Although the role of the IL-17 pathway in malignancy risk is not well characterized, potential malignancies are considered an event of interest with immunomodulatory biologics. Among patients with rheumatoid arthritis in a large cohort study, use of tumor necrosis factor inhibitors was associated with increased risk of nonmelanoma skin cancer (NMSC). Traditional therapies for psoriasis such as cyclosporine may also increase risk of NMSC and other malignancies including lymphoma.

**OBJECTIVE:** To summarize malignancy rates from clinical studies of brodalumab.

**METHODS:** Data were pooled from phase 2 trials and 3 large, multicenter, randomized phase 3 trials of brodalumab in moderate-to-severe plaque psoriasis (including AMAGINE-2/-3, in which patients were randomized to...
brodalumab, ustekinumab, or placebo). All adverse events (AEs) in the neoplasms benign, malignant, and unspecified (including cysts and polyps) System Organ Class were reviewed, and events were adjudicated for confirmation. Events were further categorized as Surveillance, Epidemiology, and End Results (SEER)-adjudicated malignancies (excluding basal cell carcinoma and squamous cell carcinoma of the skin, in situ cancers [except for urinary bladder], benign neoplasms, and recurrent tumors) and NMSCs. Data from the 52-week (brodalumab and ustekinumab) and long-term (brodalumab) pools were summarized as exposure- or time-adjusted event rates per 100 patient-years (PY).

RESULTS: Exposure-adjusted event rates at 52 weeks were somewhat lower in the brodalumab group (n=4019; 3446 total PY of exposure) versus the ustekinumab group (n=613; 495 total PY of exposure), including adjudicated malignancies (0.9 [30 events] versus 2.6 [13 events]), SEER-adjudicated malignancies (0.3 [10 events] versus 0.4 [2 events]), and NMSCs (0.6 [20 events] versus 2.2 [11 events]). Most of the malignancy AEs were of grade ≤2 severity. The exposure-adjusted event rate of SEER-adjudicated malignancies in the brodalumab group remained stable in the long-term analysis (0.3 [26 events]) and was consistent with the time-adjusted event rate (0.4 [37 events]).

CONCLUSION: The rates of malignancy in clinical studies of brodalumab were generally low. There was no increased risk of malignancy with brodalumab relative to ustekinumab through 52 weeks. Longer follow-up time is needed to fully characterize the risk of malignancy with brodalumab.

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DISCLOSURES: Mark Lebwohl is an employee of Mount Sinai, which receives research funds from AbbVie, Inc; Bausch Health; Boehringer Ingelheim; Celgene Corporation; Eli Lilly & Co; Incyte; Janssen/Johnson & Johnson; LEO Pharma; MedImmune/AstraZeneca; Novartis; Pfizer, Inc; ScIderm; UCB; and ViDac and is also a consultant for Allergan; Aqua; Arcutis; Boehringer Ingelheim; LEO Pharma; Menlo; and Promius. Kenneth Gordon has received research support from AbbVie, Inc; Amgen, Inc; Boehringer Ingelheim; Celgene Corporation; and Eli Lilly & Co and has served as a consultant for AbbVie, Inc; Amgen, Inc; Boehringer-Ingelheim; Celgene Corporation; Dermira, Inc; Eli Lilly & Co; Novartis AG; and Pfizer, Inc.

Lawrence Green has served as an investigator, consultant, or speaker for Amgen, Inc; AbbVie, Inc; Celgene Corporation; Janssen Biotech, Inc; Novartis Pharmaceuticals Corporation; Sun Pharmaceutical Industries Ltd; and Bausch Health. Radhakrishnan Pillai is an employee of Dow Pharmaceutical Sciences and holds stock and/or stock options in the company. Abby Jacobson is an employee of Ortho Dermatologics and holds stocks and/or stock options in Bausch Health.

FUNDING: This study was sponsored by Ortho Dermatologics. Medical writing and editorial assistance, funded by Ortho Dermatologics, were provided by MedThink SciCom.

PA-45: Mirtazapine Induced Severe Steven-Johnson Syndrome/Toxic Epidermal Necrolysis

ABSTRACT: We present a 43-year-old male who presented with 5 days of dry cough, 2 days of intermittent high fevers, altered mental status, and sloughing of his skin. Per the family who gave most of the history, he had recently been started on an antidepressant by his primary care physician after a year of counseling had not shown significant improvement in his mood. The cough started insidiously but just prior to presentation he was coughing almost continuously and spitting out what appeared to be chunks of his oral cavity mucosa per family. This was accompanied by the fevers which were measured up to 102 F, and in the past day, he was very confused about where he was and who the people around him were.

He was hemodynamically unstable at presentation with systolic pressures in the 70s, and required vasopressor support for a presumed septic shock. He was taken to the medical intensive care unit and started on empiric antibiotics as well. A lumbar puncture was obtained for ruling out meningitis, and fluid, blood, urine, and sputum cultures were sent. During the initial management, he had to be intubated for airway protection given continuous sloughing of oral mucosa and bleeding. A skin biopsy was performed and showed “pericapillary mononuclear infiltrate in the papillary dermis composed of T cells and scant apoptotic keratinocytes,” confirming the diagnosis of Steven-Johnson’s Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN). His Score of TEN (SCORTEN) was found to be 5, which correlated to less than one fourth survival rate, and he was started on early cyclosporine therapy. On obtaining his home medications, he was found to have been started on mirtazapine at the most recent primary care visit a week prior to presentation.

Further hospital course was complicated. The patient was managed in the burn unit, treated with antibiotics till cultures returned negative. The primary focus was on wound care, fluid and electrolyte management, nutritional support, ocular care, temperature management, and pain control, among others. For this, various services remained in the care team including Dermatology, wound care, burn surgery, nephrology, and nutrition. Ocular care was done with topical steroid and antibiotic combination with saline irrigation in between. He was being monitored keenly for infective complications as well but fortunately, did not develop any further fevers.
after discontinuation of the initial empiric antibiotics. The respiratory status was a bigger problem for the care team. Because of continuous sloughing of his oral mucosa, he could not be safely extubated despite having good lung mechanics.

On the second week of hospital stay, he started to slow down with the oral mucosal sloughing. The sedation was stopped, he started responding appropriately to commands and had good cough and gag reflexes. After a successful trial of spontaneous breathing, he was extubated to room air. He had no further complications and the skin slowly healed with some scarring. He was eventually discharged home with dermatology and primary care follow up and was advised to avoid mirtazapine. He was given a list of the most common medications to avoid and this was circulated with the entire care team.

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PA-46: Multicenter Pivotal Study of the Safety and Effectiveness of a Tissue Stabilized-Guided Subcision Procedure for the Treatment of Cellulite- 5 Year Update

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BACKGROUND: Tissue release (subcision) for cellulite has been practiced for decades with limited success. A novel procedure has been developed which stretches and stabilizes tissue while providing integrated anesthesia delivery and precise depth control of minimally-invasive tissue release.

OBJECTIVE: The pivotal study supported the FDA-clearance of this novel tissue stabilized-guided subcision (TS-GS) system as an effective and safe treatment for the long term improvement in the appearance of cellulite in the buttocks and thighs with no diminishment of benefit for up to 3 years. The purpose of this study update was to determine the safety and efficacy of TS-GS for maintained improvement in the appearance of cellulite of the buttocks and thighs out to 5 years.

METHODS: A pivotal prospective multi-center safety and effectiveness study enrolled 55 subjects. Subjects underwent a single treatment, and were followed at regular intervals out to 5 years. Safety was assessed and effectiveness was evaluated by blinded, independent physician evaluators using randomized (before and after) professional photographs and a novel, validated 6 point (0-5) cellulite severity scale.

RESULTS: Treatments were well tolerated with minor expected side effects that resolved quickly. Improvement was rapid and pronounced. 37 subjects completed 5-year follow-ups. Five-year average reduction in cellulite severity was 1.8 points (p<0.0001), and masked evaluator improvement was 92.8%. At 5 years, evaluators rated 100% of subjects as having noticeable improvement and 78.4% of subjects were either satisfied or very satisfied.

CONCLUSION: Tissue release at precise depths leads to significant, lasting improvement in cellulite. The results of this study demonstrates that a single treatment with a novel TS-GS release system improved the appearance of cellulite on the thighs and buttocks through 5 years of follow-up with minimal adverse effects.

DISCLOSURES: All authors have been consultants and/or investigators for Merz North America, Inc. This study was sponsored by Merz North America, Inc.

PA-47: Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to- Severe Acne Vulgaris: Assessment of Safety and Tolerability in Subgroups

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DISCLOSURES: JAZ, JCH, and WER are advisors to Ortho Dermatologics. EG, VB, and RP are employees of Bausch Health.

BACKGROUND: Topical tretinoin has been extensively studied in clinical trials, and its essential role in the treatment of acne vulgaris (acne) established through evidence-based guidelines. However, there is a common perception that its use is associated with significant cutaneous irritation, and the potential to cause or exacerbate postinflammatory hyperpigmentation (PIH) in those patients especially vulnerable (ie., Hispanics and African Americans). A novel tretinoin 0.05% lotion was developed using polymerized emulsion technology to provide both improved efficacy and tolerability.

OBJECTIVE: To evaluate safety and tolerability of a novel tretinoin 0.05% lotion in moderate-to-severe acne.

METHODS: A total of 1640 patients, 9 to 58 years of age, were randomized to receive a novel tretinoin 0.05% lotion or vehicle in two double-blind, placebo-controlled 12-week, 2-arm, parallel group studies evaluating safety and efficacy. Cutaneous safety (erythema and scaling) and the potential to cause or exacerbate postinflammatory hyperpigmentation (PIH) in those patients especially vulnerable (ie., Hispanics and African Americans). A novel tretinoin 0.05% lotion was developed using polymerized emulsion technology to provide both improved efficacy and tolerability.

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METHODS: A total of 1640 patients, 9 to 58 years of age, were randomized to receive a novel tretinoin 0.05% lotion or vehicle in two double-blind, placebo-controlled 12-week, 2-arm, parallel group studies evaluating safety and efficacy. Cutaneous safety (erythema and scaling) and the potential to cause or exacerbate postinflammatory hyperpigmentation (PIH) in those patients especially vulnerable (ie., Hispanics and African Americans). A novel tretinoin 0.05% lotion was developed using polymerized emulsion technology to provide both improved efficacy and tolerability.
summarized by treatment group, severity, and relationship to study treatment.

RESULTS: Across the two studies, tretinoin 0.05% lotion was considered safe and very well tolerated. The most commonly reported treatment-related AEs were of low incidence and included application site reactions, and skin-related events attributed to the known properties of tretinoin. Only application site pain (3.1%), dryness (3.7%), and erythema (1.4%) were reported by >1% of patients. Skin reactions (such as scaling, burning, and stinging) were rare, mild, and transient. Application site reaction scores were lower than those reported in studies with other tretinoin formulations (eg, microsphere, gel), even in those patients (ie, pediatrics and females) known to be more susceptible to irritation (incidence 1.4% and 1.2%, respectively). In those patients where PIH may be more of a concern than the acne that proceeds it, mean baseline scores were reduced with treatment.

LIMITATIONS: This subgroup analysis is post hoc.

CONCLUSIONS: This novel tretinoin 0.05% lotion developed using polymerized emulsion technology provides a highly favorable safety and tolerability profile in moderate-to-severe acne patients.

PA-48: Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in an Adult and Adolescent Female Population

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DISCLOSURES: LHK is an advisor with Ortho Dermatologics and investigator with Dow Pharmaceutical Sciences. HB is an investigator with Dow Pharmaceutical Sciences. EG and VB are employees of Bausch Health.

BACKGROUND: Acne vulgaris (acne) is a common dermatological condition typically associated with adolescents, affecting about 85% of young people. However, it is also prevalent and persistent into adulthood, particularly in females. The efficacy of tretinoin in acne is well documented with large pivotal studies. The first lotion formulation of tretinoin was developed to provide an important alternative option to treat acne patients who may be sensitive to the irritant effects of other tretinoin formulations.

OBJECTIVE: To determine efficacy and safety of tretinoin 0.05% lotion in a female population with moderate-to-severe acne and whether findings were similar in adolescent (<18 years) and adult (≥18 years) women.

METHODS: A post hoc analysis of two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies in moderate or severe acne was performed. Female patients (aged 9 to 58 years, N=909) randomized (1:1) to receive tretinoin 0.05% lotion or vehicle, once-daily for 12 weeks. Efficacy assessments included changes in baseline inflammatory and non-inflammatory lesions and treatment success (at least 2-grade reduction in Evaluator’s Global Severity Score [EGSS] and clear/almost clear). Safety, adverse events (AEs) and cutaneous tolerability were evaluated throughout.

RESULTS: At Week 12, mean percent reduction in inflammatory and non-inflammatory lesion counts were 56.9% and 51.7%, respectively, compared with 47.1% and 34.9% with vehicle (P<0.001) in the overall female population. Similar results were seen in adult and adolescent females in terms of reduction in inflammatory lesion counts with tretinoin 0.05% lotion; but the reduction in non-inflammatory lesions was significantly greater in adult females (P=0.002). Treatment success was achieved by 23.6% of patients by Week 12, compared with 13.5% on vehicle (P<0.001). Although treatment success was greater in adult females (24.6% versus 21.6%), the difference was not significant. The majority of AEs were mild and transient. There were five serious AEs (SAEs) reported (4/1, adult/adolescent, respectively). The most frequently reported treatment-related AEs with tretinoin 0.05% lotion were application site pain (3.0%/5.7%), and application site dryness (4.9%/6.4%). Local cutaneous safety and tolerability assessments were generally mild-to-moderate and improved by Week 12. Slight increases in mean scores were observed for scaling, burning, and stinging within the first 4 weeks and appeared to be transient.

LIMITATIONS: This is a post hoc analysis.

CONCLUSIONS: Tretinoin 0.05% lotion was significantly more effective than its vehicle in achieving treatment success and reducing inflammatory and non-inflammatory lesions in female acne. Non-inflammatory lesion count reduction was significantly greater in adult females than the adolescent females. The new lotion formulation was well-tolerated, and all treatment-related AEs were both mild and transient in nature.

PA-49: Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in a Preadolescent Population

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DISCLOSURES: LFE and JLS are advisors to Ortho Dermatologics and investigators with Dow Pharmaceutical Sciences. EG and VB are employees of Bausch Health.

BACKGROUND: Acne vulgaris (acne) is one of the most common skin conditions in children and adolescents. The efficacy of tretinoin is well documented with large pivotal studies that included pediatric patients ranging from 12 to 18 years of age. With acne routinely presenting in patients younger than 12 years, data are needed in a younger age group. Lotion formulations are commonly used across dermatology and are well-liked by patients. The first lotion formulation of tretinoin was developed to provide an important alternative option to treat acne patients who may be sensitive to the irritant effects of other tretinoin formulations.

OBJECTIVE: To evaluate the safety and efficacy of a novel once-daily application of a tretinoin 0.05% lotion in preadolescent patients aged ~13 years with moderate-to-severe acne.

METHODS: Post hoc analysis of two multicenter, randomized, double-blind, vehicle-controlled Phase 3 studies in moderate or severe acne. Preadolescent patients (aged 9 to 13 years, N=154) were randomized (1:1) to receive tretinoin 0.05% lotion or vehicle, once-daily for 12 weeks. Efficacy assessments included changes in baseline inflammatory and non-inflammatory lesions and treatment success (at least 2-grade reduction in Evaluator’s Global Severity Score [EGSS] and clear/almost clear). Safety, adverse events (AEs), and cutaneous tolerability were evaluated throughout.

RESULTS: At Week 12, mean percent reduction in inflammatory and non-inflammatory lesion counts were 49.5% and 44.0%, respectively, compared with 31.4% and 18.8% with vehicle (both P=0.001). Treatment success was achieved by 23.7% of patients by Week 12, compared with 7.2% (P=0.009). The majority of AEs were mild and transient. There were no serious AEs (SAEs) reported. The most frequently reported treatment-related AEs with tretinoin 0.05% lotion were application site pain (5.6%), and application site dryness (2.8%). Local cutaneous safety and tolerability assessments were generally mild-to-moderate and improved by Week 12. Slight increases in mean scores were observed for scaling, burning, and stinging within the first four weeks and appeared to be transient.

LIMITATIONS: This is a post hoc analysis.

CONCLUSIONS: Tretinoin 0.05% lotion was significantly more effective than its vehicle in achieving treatment success and reducing inflammatory and non-inflammatory lesions in preadolescent acne. The new lotion formulation was well-tolerated, and all treatment-related AEs were both mild and transient in nature.

PA-50: Optimizing Patient Outcomes Through a Customized Approach of Microfocused Ultrasound with Visualization Treatments: Consensus Guidelines

Sabrina Fabi, MD, on behalf of the Consensus Group

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BACKGROUND: Microfocused ultrasound with visualization (MFU-V) is FDA-cleared for the lifting the skin of the brow, neck, and submentum, as well as for improvement of lines and wrinkles of the décolleté.

OBJECTIVE: The aim of these consensus guidelines is to provide a framework for a customized treatment plan informed by key patient characteristics and proper use of MFU-V to assess skin anatomical features.

DESIGN: Consensus guidelines were developed by a global panel of expert aesthetic physicians for the use of MFU-V. Key discussion topics included: patient factors that contribute to favorable or poor outcomes; customization of the number of treatment lines, energy settings, and treatment depths; distinguishing approaches for restorative, preventative, and maintenance treatments; and important safety considerations.

SUMMARY: Use of MFU-V is the most important factor for selecting transducers/treatment depth and planning the number of lines at each depth. Higher density treatments are associated with ideal outcomes. Treatment intervals should be tailored to age, with older patients requiring more frequent treatments to maintain results driven by continued collagen production. Because neo-collagenesis is valuable to all patients, MFU-V can be applied for both preventative and restorative treatments. In addition to proper technique, the most important factors associated with positive outcomes are management of patient expectations and proper diagnosis.

CONCLUSION: Supported by a large body of literature, a well-characterized mechanism of action, and high reported patient satisfaction, MFU-V is considered by the panel to be a key aesthetic treatment and the gold standard for nonsurgical lifting and tightening of the skin. These guidelines expand upon available evidence and clinical data to provide a framework for physicians to fully customize their approach with MFU-V, leading to favorable outcomes that are integral to a patient’s overall aesthetic treatment plan.

DISCLOSURES: Dr Fabi has been a consultant and investigator for Merz North America, Inc. This study was sponsored by Merz North America, Inc.

PA-51: Pachyonychia Congenita Tarda Presenting with Solitary Plantar Keratoderma and Keratin 16 Mutation

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BACKGROUND: Pachyonychia congenita (PC) is an autosomal dominant keratinizing disorder characterized by palmoplantar keratoderma, variable hypertrophic nail dystrophy, and debilitating plantar pain typically apparent soon after birth. Rarely, patients present in adulthood
(pachyonychia congenital tarda, PCT), posing a formidable diagnostic challenge.

**CASE:** A 46-year-old African American female presented with 4 months of progressively worsening painful plantar plaques. Symptoms started after long periods standing as a cashier. Family history was negative for similar features. The plantar surfaces had thick skin-colored plaques extending to the hyponychium and interdigital spaces with fissures, without palpable involvement. Lesions were not confined to points of pressure. Histology demonstrated verruciform change with broad orthokeratotic hyperkeratosis consistent with plantar keratoderma. Topical clobetasol-tar-salicylic acid resulted in improvement with plaque softening and sloughing. The adult onset of her skin findings in the setting of a strong family history of multiple malignancies was concerning for acquired plantar keratodermas—particularly Howel-Evans syndrome, which is accompanied by a 95% risk of developing esophageal cancer. Gene sequencing revealed no mutation in the RHBDF2 gene, but demonstrated a KRT16 gene mutation, securing the diagnosis of PC.

**OBJECTIVES:** 1 – To review the diagnostic considerations of adult-onset plantar keratoderma. 2 – To document a potentially unique case of pachyonychia congenita tarda that presented with solitary plantar keratoderma and none of the other common features of PC and presenting much later in life than is typical for this condition.

**METHODS/RESULTS:** N/A as this is a case report.

**LIMITATIONS:** This is a case report and has very limited power.

**CONCLUSION:** The original series reporting PCT and subsequent cases document isolated nail findings or a constellation of palmoplantar keratoderma, leukokeratosis, and cutaneous cysts [2, 3]. As of 2017, registry data shows 98% of patients with KRT16 mutation develop plantar keratoderma before age 15 [4]. Our patient presents a potentially unique case of PCT manifesting only with plantar keratoderma, lacking the other common features of PC (hypertrophic nail dystrophy, follicular hyperkeratosis, and oral leukokeratosis) and also presenting much later in life than is typical for this condition.

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**DISCLOSURES:** Neither I nor my institution at any time received payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, and statistical analysis). There were no other relevant financial relationships that have an interest in the content of the submitted work. I have no relevant non-financial associations or interests that a reasonable reader would want to know about in relation to the submitted work.

**PA-52: Patient Characteristics and Treatment Patterns for Patients Initiating Ixekizumab: Findings from the Corrona Registry**

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**BACKGROUND:** Psoriasis is a chronic, immune-mediated disease whose key clinical symptoms include skin itching, pain, and scaling. Many psoriasis patients have reported decreases in their quality of life (QoL) and work productivity. Ixekizumab is a high affinity fully human monoclonal antibody that selectively neutralizes IL-17A, and clinical trials have shown significant efficacy in the treatment of moderate to severe psoriasis (PsO) and psoriatic arthritis (PsA). Limited data are available on its effectiveness in a real-world setting.

**OBJECTIVE:** The objective of the study was to provide a description of real-world treatment patterns among ixekizumab patients in terms of drug survival, drug discontinuation, drug switching, and the corresponding reasons for these changes.

**METHODS:** Using the Corrona Psoriasis Registry, an independent, prospective observational cohort of patients aged 18 or older launched in April 2015, we provide descriptive statistics for real-world treatment patterns among ixekizumab patients at 6-month follow-up.

**RESULTS:** As of May 10, 2018, there were 136 ixekizumab users at enrollment within the PsO registry who had a 6-month follow-up visit available. The mean age (SD) at enrollment was 50.8 (13.0). 53% of patients were male, and the mean BMI (SD) was 32.0 (8.2). The most common comorbidity was hypertension (40%) followed by hyperlipidemia (30%), anxiety (26%), and depression (22%). Nearly the entire population suffered with plaque PsO (99%), and 38% had scalp involvement. The mean (SD) duration since onset of PsO was 17.8 (14.0) years, and 45% of patients had PsA. Most of the patients were biologic experienced (83%). The median (IQR) prior biologic usage was 2 (1.0, 3.0) biologics, and the median prior non-biologic use was 1 (1.0, 2.0). Most patients (86%) remained on therapy over the study period, 10% discontinued therapy without starting another treatment, and 4% switched treatment. The mean time on ixekizumab for those discontinuing was 2.9 months, and the mean time for those switching from ixekizumab was 4.2 months. The most common reasons for starting ixekizumab at enrollment were active disease (84%), followed by non-clinical reasons (8%) (ie, patient preference, frequency of administration, patient cost), lack of effect (2%), doing well (1%), and other reasons (4%) (ie, compliance, tolerability, administration
route, mechanism of action, denied by insurance, temporary interruption, other). The number of patients who stopped or switched is quite small, 13 patients and 6 patients, respectively. The most common reasons cited for stopping therapy were other reasons (n=7), effect of (n=4), side effects (n=3), and doing well (n=1). The reasons cited for switching therapy were either non-clinical reasons (n=2) or other reasons (n=5). When conducting subgroup analyses, we saw similar patterns when the data was stratified by body weight (<100 kg vs ≥100 kg) or the presence or absence of PsA.

CONCLUSIONS: In conclusion, in a psoriasis population with high previous biologic use, 86% of ixekizumab initiators had no change in therapy at 6-month follow-up, while patients who discontinued (10%) and switched (4%) were minimal.

**PA-53: Phase 1 Study of Cemiplimab, a Human Monoclonal Anti-PD-1, in Patients with Unresectable Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma (CSCC): Longer Follow-Up Efficacy and Safety Data**

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**BACKGROUND:** Cemiplimab (REGN2810) demonstrated a positive risk/benefit profile and produced antitumor activity in patients (pts) with advanced CSCC in the primary analysis, by independent central review, of a phase 1 CSCC expansion cohorts (ECs). We now report longer follow-up data from the CSCC ECs of the phase 1 study (NCT02383212).

**METHODS:** Pts with distantly metastatic or locally/regionally advanced CSCC who were not candidates for surgery were enrolled in ECs 7 and 8, respectively. All pts received cemiplimab 3 mg/kg by intravenous infusion over 30 minutes every 2 weeks for up to 48 weeks. Tumor measurements were performed every 8 weeks by RECIST 1.1 to determine overall response rate (ORR; complete response [CR] + partial response [PR]) according to intention to treat. The data cut-off date was Jan 20, 2018. Tumor response in this report was by investigator assessment.

**RESULTS:** A total of 26 pts were enrolled (21 M/5 F; 10 in EC 7, 16 in EC 8; median age: 72.5 years [range: 55–88]; ECOG performance status was 1 in 16 pts and 0 in 10 pts). Median duration of follow-up was 11.9 months (range: 1.1–18.2). Median duration of cemiplimab exposure was 36.0 weeks. The most common treatment-emergent adverse event (TEAE) of any grade was fatigue (26.9%). The only TEAEs of grade ≥3 that occurred in more than one pt were hypercalcemia and skin infection (each 7.7%). ORR was 50.0% (95% CI: 29.9–70.1), with 2 CRs and 11 PRs; 5 patients had stable disease (SD), 6 had progressive disease, and 2 were not evaluable for response. Durable disease control rate (SD or response for ≥105 days) was 57.7% (95% CI: 36.9–76.6). The median time to response was 1.9 months (range: 1.7–7.5). The median duration of response has not been reached, and as of the data cut-off date, for pts with CR or PR, the observed duration of response exceeded 6 months in 9 pts and 12 months in 5 pts.

**CONCLUSIONS:** The increasing duration of response in this analysis provides further evidence of a positive risk/benefit profile for cemiplimab in pts with advanced CSCC.

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**ACKNOWLEDGMENTS:** The study was sponsored by Regeneron Pharmaceuticals, Inc. and Sanofi. Medical writing support under the direction of the authors was provided by Emmanuel Ogunnowo, PhD, of Prime (Knutsford, UK) and funded by Regeneron Pharmaceuticals, Inc. and Sanofi according to Good Publication Practice guidelines (Link).

**DISCLOSURES:** Taofeek K. Owonikoko has received fees for consulting or advisory role for Novartis, Celgene, Lilly, Sandoz, Abbvie, Eisai, G1 Therapeutics, Takeda, Seattle Genetics, Bristol-Myers Squibb, MedImmune. Kyriakos P. Papadopoulos declares no conflict of interest. Melissa L. Johnson declares no conflict of interest. Marta Gil-Martin declares no conflict of interest. Victor Moreno declares no conflict of interest. April K. Salama has received fees for consulting or advisory and speakers’ bureau roles for Bristol-Myers. Emiliano Calvo has received research funding from Boehringer Ingelheim, Roche/Genentech, BMS, Novartis, PsoIoxus, Nanobiotix, Janssen, Abbvie, PharmaMar, PUMA, Sanofi, Lilly, Pfizer, Merck, Nektar, Amcure, Amgen, AstraZeneca, Principia, Bayer, CytomX, H3, Incyte, Kura, LOXO, Macrogenics, Menarini, Merck, Merus, Millenium, Rigontec, Takiho, TesaroReceipt, and has received honoraria or...
consultation fees from Novartis, Nanobiotix, Janssen-Cilag, PsiOxus Therapeutics, Seattle Genetics, Pierre Fabre, Boehringer Ingelheim, Cerulean Pharma, EUSA, Abbvie, Celgene. He has received speaker’s bureau fees from Novartis. Nelson S. Yee has received institutional research funding from Boston Biomedical Inc., Merck and Co. Inc., Pharmacies, and Regeneron Pharmaceuticals, Inc., as well as travel/accommodation expenses from Daiichi Sankyo, Foundation Medicine, and Caris Life Sciences. Howard Safran declares no conflict of interest. Raid Aljumaily declares no conflict of interest. Daruka Mahadevan has received speakers’ bureau and travel and accommodation expenses from Abbvie. Jiaxin Niu has received consulting or advisory role fees from Genentech, Biodexis, Paradigm, Ignyta, AstraZeneca, and Teueda. KosaiAl Kal Mohan is an employee and shareholder of Regeneron Pharmaceuticals, Inc. Jingjin Li is an employee and shareholder of Regeneron Pharmaceuticals, Inc. and Novartis. Elizabeth Stankevich is an employee of Regeneron Pharmaceuticals, Inc., and a shareholder of Regeneron Pharmaceuticals, Inc., Celgene, Bristol-Myers Squibb, and Merck. Melissa Mathias is a shareholder and an employee of Regeneron Pharmaceuticals, Inc., Israel Lowy is an employee of, shareholder of, and gained fees for travel and accommodation expenses as well as leadership from Regeneron Pharmaceuticals, Inc. Matthew G. Fury is an employee of and shareholder in Regeneron Pharmaceuticals, Inc., and has patents, royalties, and other intellectual property from Regeneron Pharmaceuticals, Inc. Hani M. Babiker has received honoraria from Bayer and Sirtex, and consulting or advisory role fees from Celgene and Endocyte.

PA-54: Phase 2 Study of Cemiplimab, a human Monoclonal Anti-PD-1, in Patients With Advanced Basal Cell Carcinoma (BCC) Who Experienced Progression of Disease on, or Were Intolerant of Prior Hedgehog Pathway Inhibitor (HHI) Therapy

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INTRODUCTION: BCC is the most common cancer worldwide. There is no approved agent to treat advanced BCC in patients who experience disease progression on, or who are intolerant of, HHIs. Cemiplimab (REGN2810), an anti-PD-1, has demonstrated encouraging efficacy and favorable tolerability in a phase 1 study of patients with advanced malignancies (NCT02383212).

MATERIALS, METHODS, & STUDY OBJECTIVES: We are conducting a phase 2, non-randomized, 2-group, multi-center study of cemiplimab in patients with advanced BCC who experienced disease progression on, or are intolerant to, HHI therapy (NCT03132636). Group 1 will enroll patients with both nodal and distant metastatic BCC. Group 2 will enroll patients with locally advanced BCC who are not candidates for surgery or radiotherapy. Cemiplimab will be administered intravenously every 3 weeks in all patients. The primary objective of the study is to evaluate overall response rate (ORR) as determined by central review. The ORR will be assessed separately for patients in Group 1 or Group 2 (by RECIST 1.1 for radiology, and modified WHO for photography). Up to 137 patients will be enrolled. For Group 1, 50 patients are required to provide at least 85% power to reject a null hypothesis of an ORR of 15% at a 2-sided significance level of 5% if the true ORR is 34%. For Group 2, 80 patients are required to provide at least 85% power to reject a null hypothesis of an ORR of 20% at a 2-sided significance level of 5% if the true ORR is 35%. An additional 5% in sample size will account for patient withdrawals. This study is ongoing.

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PA-55: Primary Analysis of Phase 2 Results for Cemiplimab, a Human Monoclonal Anti-PD-1, in Patients with Metastatic Cutaneous Squamous Cell Carcinoma (mCSCC)

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BACKGROUND: CSCC is second the most common skin cancer after basal cell carcinoma. There is no standard of care for patients with mCSCC. Cemiplimab (REGN2810) treatment at 3 mg/kg every 2 weeks (Q2W) demonstrated encouraging preliminary activity in CSCC in a phase 1 study. We present the primary analysis of the mCSCC cohort from the pivotal phase 2 study (NCT02760498; data cut-off date: Oct 27, 2017).

METHODS: Patients with mCSCC (defined as nodal and/or distant) received cemiplimab 3 mg/kg Q2W intravenously over 30 minutes. Tumor measurements were performed Q8W. The primary objective was to evaluate overall response rate (ORR; complete response [CR] + partial response [PR]) according to independent central review (per RECIST 1.1 for scans; modified WHO criteria for photos). Duration of response (DOR) was a key secondary endpoint. Durable disease control rate (DDCR) was defined as stable disease or response for ≥16 weeks.

RESULTS: 59 patients were enrolled (54 M/ 5 F; median age: 71.0 years [range: 38–93]; ECOG performance status: 0 and 1 in 23 and 36 patients, respectively). 33 patients (55.9%) had received prior systemic therapy, and 50 (84.7%) had received prior radiotherapy. Median duration of follow-up was 7.9 months (range: 1.1–15.6). ORR by central review was 47.5% (95% CI: 34.3–60.9; 4 CRs and 24 PRs). Responses were observed irrespective of prior systemic therapy. Median DOR has not been reached. Only 3 responding patients had subsequent disease progression at the time of data cut-off. DDCR was 61% (95% CI: 47.4–73.5). Median time to response was 1.9 months (range: 1.7–6.0). The most common adverse events (AEs) regardless of attribution (all grades, ≥Grade 3) were diarrhea (27.1%, 1.7%), fatigue (23.7%, 1.7%), and nausea (16.9%, 0.0%). Immune-related AEs ≥Grade 3 (per investigator assessment) occurred in 10.2% of patients.

CONCLUSIONS: In the largest prospective study reported in patients with mCSCC, cemiplimab 3 mg/kg Q2W showed substantial activity and durable responses. The safety profile was comparable with other anti-PD-1 agents.

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DISCLOSURES: Danny Rischin: reports institutional clinical trial funding from Regeneron Pharmaceuticals, Inc., during the conduct of the study; institutional clinical trial funding and grants from Roche Genentech and GSK; and institutional clinical trial funding and uncompensated scientific committee and advisory board from Merck (MSD), Bristol-Myers Squibb, and Amgen. Michael R. Migden: reports honoraria/travel expenses from Regeneron Pharmaceuticals, Inc., Novartis, Genentech, Eli Lilly, and Sun Pharma; and institutional research funding from Regeneron Pharmaceuticals, Inc., Novartis, Genentech, and Eli Lilly. Anne Lynn S. Chang: reports grant from Regeneron Pharmaceuticals, Inc., during the conduct of the study. Christine H. Chung: reports institutional research funding from Regeneron Pharmaceuticals, Inc., during the conduct of the study; and personal fees from Bristol-Myers Squibb and Astra Zeneca. Lara A. Dunn: reports institutional fees from Regeneron Pharmaceuticals, Inc., during the conduct of the study, as well as research support from Eisai Pharmaceuticals. Alexander Guminiski: reports personal fees and non-financial support (advisory board and travel support) from BMS and Sun Pharma; personal fees (advisory board) from Merck KgA, Eisai, and Pfizer; non-financial (travel) support from Astellas, and clinical trial unit support from PPD Australia. Axel Hauschild: reports institutional grants, speaker’s honoraria, and consultancy fees from Amgen, Bristol-Myers Squibb, MSD/Merck, Pierre Fabre, Provectus, Roche, and Novartis; institutional grants and consultancy fees from Merck Serono, Philogen, and Regeneron Pharmaceuticals, Inc.; and consultancy fees from OncoSec. Leonel Hernandez-Aya: reports institutional fees from Regeneron Pharmaceuticals, Inc., during the conduct of the study; institutional fees from BMS, Merck, Amgen, Roche, Novartis, Immunocore, Merck-EMD, Corvus, Polynoma, and Genentech. Brett G.M. Hughes: reports participation as advisory board member for Bristol-Myers Squibb, Borrhinger Ingelhiem, Merck Sharp & Dohme, Roche, AstraZeneca, Pfizer, and Eisai. Karl D. Lewis: reports grant and consulting fees from Regeneron Pharmaceuticals, Inc. during the conduct of the study. Annette M. Lim: was supported by the Department of Health (W.A)/Raine Medical Research Foundation Clinician Research Fellowship. Badri Modi: declares no conflict of interest. Dirk Schadendorf: reports institutional patients’ fees from Regeneron Pharmaceuticals, Inc., during the conduct of the study; adboard honorarium fees Amgen and Leo
Pharma; speaker fee from Boehringer Ingelheim; adboard, speaker honorarium and patients’ fees from Roche, Novartis, BMS, and Merck-EMD; adboard and speaker honorarium fees from Incyte and Pierre Fabre; adboard honorarium, and patients’ fees from MSD, steering cie honorarium fees from 4SC, adboard fees from AstraZeneca, Pfizer, and Array; and adboard and patients’ fees from Philogen. Chrysalyn D. Schmults: reports participating as steering committee member with Castle Biosciences, grants (basal cell staging) from Genentech, grants (cutaneous squamous cell carcinoma [Investigational programmed cell death-1 drug]) from Regeneron Pharmaceuticals, Inc., outside the submitted work. Jocelyn Booth: is an employee of Regeneron Pharmaceuticals, Inc. Siyu Li: is an employee of Regeneron Pharmaceuticals, Inc. Kosalai Mohan: is an employee of Regeneron Pharmaceuticals, Inc. Elizabeth Stankevich: is an employee and shareholder of and has received accommodation and travel expenses from Regeneron Pharmaceuticals, Inc. Israel Lowy: is an employee, has been compensated for leadership roles, is a shareholder of, and has received fees for accommodation and travel expenses from Regeneron Pharmaceuticals, Inc. Matthew Fury: is an employee and shareholder of and has received fees for patents, royalties, or other intellectual property and accommodation and travel expenses from Regeneron Pharmaceuticals, Inc.

**PA-56: Primary Efficacy and Safety of Adalimumab in Nail Psoriasis from the First 26 Weeks of a Phase-3, Randomized, Placebo-Controlled Trial with Subanalysis in Patients with and without Psoriatic Arthritis**

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**INTRODUCTION:** Psoriasis (Ps) disease burden for patients with psoriasis (Ps) and concomitant fingernail Ps plus psoriatic arthritis (PsA) is higher compared with patients with Ps alone. We report safety and efficacy of originator adalimumab (ADA) in patients with fingernail Ps, and also for patients with or without concomitant PsA.

**METHODS:** Results are reported from the double-blind PBO-controlled, Period A in which 217 patients with moderate to severe plaque Ps and fingernail Ps were included and randomized 1:1 to receive 40 mg ADA every other week (eow) from week 1 (initial 80mg dose at week 0), or matching PBO, for 26 weeks. The primary endpoints were the proportion of patients with ≥75% improvement in modified Nail Ps Severity Index (mNAPSI 75) and the proportion of patients with Physician’s Global Assessment of Fingernail Psoriasis (PGA-F) of clear (0) or minimal (1) with ≥2-grade reduction from baseline (primary in US only; for regulatory purposes). Missing data were handled by multiple imputations. Safety was assessed using treatment-emergent adverse events (AEs).

**RESULTS:** Of the 217 randomized patients (108 PBO, 109 ADA), 84.3% were male; mean age was 46.7 years; 188 (86.6%) completed 26 weeks of treatment or early escaped to Period B according to protocol. At baseline, 28.6% had PsA (29.6% PBO, 27.5% ADA) with mean duration 7.91 years [SD 8.314]. Total fingernail mNAPSI 75 was achieved by 0.5% PBO vs 61.5% ADA of patients with PsA and 4.6% ADA vs 40.9% ADA without PsA (p<0.001 for both groups). PGA-F 0 or 1 with ≥2-grade reduction was achieved by 4.4% PBO vs 59.3% ADA with PsA and 7.9% PBO vs 44.9% ADA without PsA (p<0.001 for both groups). Adverse events (AEs) in Period A were reported by 55.6% PBO vs 56.9% ADA (with PsA: 56.3% PBO vs 56.7% ADA; without PsA: 55.3% PBO vs 57.0% ADA without PsA); serious AEs by 4.6% PBO vs 7.3% ADA (with PsA: 9.4% PBO vs 10.0% ADA; without PsA: 2.6% PBO vs 6.3% ADA).

**CONCLUSIONS:** The results demonstrated that in this population, ADA was more effective than PBO for the treatment of fingernail Ps, and significantly improved signs and symptoms, both overall and regardless of the presence or absence of PsA; no new safety risks were identified with ADA eow treatment for 26 weeks.

**DISCLOSURES:** B Elewski received research funding for clinical research support, paid to her affiliation, from Abbvie, Amgen, Boehringer Ingelheim, Celgene, Incyte, Lilly, Merck, Novan, Novartis, Pfizer, Valeant, and Viamet. Received honoraria for consultant services from Anacor, Celgene, Lilly, Novartis, Pfizer, and Valeant. P Rich received grants for investigator services from AbbVie, Allergan, Amgen, Anacor, Cassiopea, Dusa, Eli Lilly, Galderma, Janssen, Leo, Meiji, Merck, Novartis, Pfizer, Psolar, Ranbaxy,Sandoz, and Viamet, honoraria for advisory board participation from AbbVie, Eli Lilly, Novartis, Sandoz, and Valeant, and honoraria for consultant services from AbbVie, Novartis, and Polichem. F Behrens received grants for investigator services from AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, and Sanofi, and honoraria for consultant services from Abbvie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, and Sanofi. G Guillet received honoraria from AbbVie for investigator services. Z Geng and O Reyes Servin receive a salary as AbbVie employees, and may also receive stocks and/or stock options.

**ACKNOWLEDGMENTS:** AbbVie Inc. funded this study and participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing, and approving of this publication. All authors had access to the data, and participated in the development, review, and approval, and in the decision to submit this publication. The authors would like to acknowledge
Yihua Gu for statistical support and Jody Bennett for medical writing support in the production of this abstract; both are employed by AbbVie.

PA-57: Protective and Reparative Effects of a Topical Dual Serum System Against UV-Induced Skin Damage

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ABSTRACT: Ultraviolet irradiation has been well-established to induce oxidative stress in the skin that may lead to apoptosis, DNA damage, and inflammation. To assess the protective and reparative effects against UV-induced oxidation of a novel topical dual-serum system (LVS), a pilot clinical study was conducted. LVS includes a day serum (LVD) to provide protection against environmental factors and a night serum (LVN) to support skin reparative processes, detoxification, and mitochondrial function.

Twelve subjects, aged 22-59 years, with Fitzpatrick Skin Type II completed the study. Visits occurred at baseline, day 1, and day 2. At baseline, subjects received two sets of randomized three (3x3 cm) sites on their backs: untreated/unexposed, untreated/UV-exposed, and treated/UV-exposed. MED determination was also conducted at this visit. To assess the protective effects of LVD, 2 μl/cm² LVD was applied approximately 15 minutes prior to UV exposure to the treated/UV-exposed site. To assess the reparative effects of LVN, 2 μl/cm² of LVN was applied immediately after UV exposure to the second set’s treated/UV-exposed site. Twenty-four hours after UV exposure, skin swabs were taken from the sites and analyzed for surface oxidation markers including malondialdehyde (MDA), oxidized squalene (SQOOH), catalase (CAT) and superoxide dismutase (SOD).

LVD treated sites prior to UV exposure showed significantly lower levels of MDA, SQOOH, CAT and SOD when compared to the untreated/UV-exposed sites (all p<0.0002; student’s paired t-test). LVN treated sites after UV exposure also showed significantly lower levels of all oxidation markers compared to the untreated/UV-exposed sites (all p<0.0001; student’s paired t-test). These results suggest that the dual-serum system composed of LVD and LVN, may provide both protective and reparative effects against UV-induced skin damage.

PA-58: Rapid and effective itch relief from calcipotriol plus betamethasone dipropionate foam in patients with psoriasis

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BACKGROUND AND OBJECTIVE: Itch is common in psoriasis, regardless of disease severity, and is bothersome to many patients (pts), adversely affecting HRQoL and sleep. Topical fixed-dose combination calcipotriol 50μg/g plus betamethasone dipropionate 0.5mg/g cutaneous foam (Cal/BD foam) has demonstrated superior efficacy and favorable tolerability vs Cal or BD alone and vs Cal/BD in gel and ointment formulations in psoriatic pts. Recently, Cal/BD foam demonstrated good itch relief, comparable to BD foam alone and superior to Cal foam alone. Steroid monotherapy is perceived as gold standard in itch relief. This pooled analysis evaluated the efficacy of Cal/BD foam on itch and itch-related sleep loss, as well as DLQI, and timing relative to effect on visible symptoms, vs foam vehicle (FV), through 4 weeks (wks) of treatment.

MATERIALS AND METHODS: Data from 3 phase 2/3 trials (NCT01536886, NCT01866163, NCT02132936) of Cal/BD foam vs FV and active comparators in psoriasis pts ≥18 years with mild-to-severe disease were pooled. For itch-related analyses, only pts with baseline (BL) itch VAS >40 were analyzed. For endpoints at days (D) 3 and 5, only phase 3 studies provided pt data. Efficacy endpoints included proportion of pts achieving itch reduction >40 (according to VAS, range 1–100) or ≥70% improvement in itch/itch-related sleep loss at D3, D5, Wks 1, 2, and 4, or 75% improvement in modified (excluding head) mPASI (mPASI75) from BL at Wks 1, 2, and 4.

RESULTS: Overall, 837 pts were included in the pooled analysis; 37 pts had BL itch VAS=0 (mean mPASI ± SD: 5.76 ± 3.06) and were subsequently excluded (Cal/BD foam, n=610; FV, n=190). 776 pts (97.0%) had data available at Wk 4; there were no systematic reasons for discontinuation. 484 had BL itch VAS >40 (mean mPASI ± SD: 7.83 ± 5.32). We found no correlation between itch VAS score and mPASI at BL (R²=0.021). In pts with a BL itch VAS >40, the proportion of pts achieving itch VAS reduction >40 increased through 4 wks with active treatment vs FV (Cal/BD foam: D3: 41.3% [p=0.05], D5: 57.5% [p=0.005], Wk 1: 60.1%, Wk 2: 70.1%, Wk 4: 83.0% [p<0.001]; FV: D3: 29.2%, D5: 40.2%, Wk 1: 35.5%, Wk 2: 42.5%, Wk 4: 45.8%). In pts with BL itch VAS >40, 34.2% of Cal/BD-foam-treated pts achieved ≥70% improvement in itch (Itch70) at D3, vs 22.5% of pts receiving Cal/BD foam vs FV and active comparators in psoriasis pts ≥18 years with mild-to-severe disease were pooled. For itch-related analyses, only pts with baseline (BL) itch VAS >40 were analyzed. For endpoints at days (D) 3 and 5, only phase 3 studies provided pt data. Efficacy endpoints included proportion of pts achieving itch reduction >40 (according to VAS, range 1–100) or ≥70% improvement in itch/itch-related sleep loss at D3, D5, Wks 1, 2, and 4, or 75% improvement in modified (excluding head) mPASI (mPASI75) from BL at Wks 1, 2, and 4.

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RESULTS: Overall, 837 pts were included in the pooled analysis; 37 pts had BL itch VAS=0 (mean mPASI ± SD: 5.76 ± 3.06) and were subsequently excluded (Cal/BD foam, n=610; FV, n=190). 776 pts (97.0%) had data available at Wk 4; there were no systematic reasons for discontinuation. 484 had BL itch VAS >40 (mean mPASI ± SD: 7.83 ± 5.32). We found no correlation between itch VAS score and mPASI at BL (R²=0.021). In pts with a BL itch VAS >40, the proportion of pts achieving itch VAS reduction >40 increased through 4 wks with active treatment vs FV (Cal/BD foam: D3: 41.3% [p=0.05], D5: 57.5% [p=0.005], Wk 1: 60.1%, Wk 2: 70.1%, Wk 4: 83.0% [p<0.001]; FV: D3: 29.2%, D5: 40.2%, Wk 1: 35.5%, Wk 2: 42.5%, Wk 4: 45.8%). In pts with BL itch VAS >40, 34.2% of Cal/BD-foam-treated pts achieved ≥70% improvement in itch (Itch70) at D3, vs 22.5% of pts receiving Cal/BD foam vs FV and active comparators in psoriasis pts ≥18 years with mild-to-severe disease were pooled. For itch-related analyses, only pts with baseline (BL) itch VAS >40 were analyzed. For endpoints at days (D) 3 and 5, only phase 3 studies provided pt data. Efficacy endpoints included proportion of pts achieving itch reduction >40 (according to VAS, range 1–100) or ≥70% improvement in itch/itch-related sleep loss at D3, D5, Wks 1, 2, and 4, or 75% improvement in modified (excluding head) mPASI (mPASI75) from BL at Wks 1, 2, and 4.
data only (Cal/BD foam, N=178; FV, N=52); at baseline, all pts had DLQI >5. An improvement in DLQI was observed in both treatment groups: 44.2% Cal/BD foam- and 18.3% FV-treated pts achieved DLQI 0/1 at Wk 4. Significant differences between Cal/BD foam- vs FV-treated pts were observed in those with BL DLQI >10 (N=172 vs N=50) who achieved DLQI ≤1 (25.0% vs 4.0%; p=0.001) and DLQI 0 (17.4% vs 2.0%; p=0.006) at Wk 4.

**CONCLUSIONS:** Cal/BD foam offers more rapid and effective relief from itch than FV; itch reduction is associated with significant improvements in sleep and DLQI. Cal/BD foam has a direct impact on itch relief observed before improvements in visible disease severity (mPASI).

**PA-59: Safety and Efficacy of Halobetasol Propionate 0.01% Lotion in the Treatment of Moderate-to-Severe Plaque Psoriasis: A Pooled Analysis of Two Phase 3 Studies**

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**DISCLOSURES:** JLS, JS, and PSY are advisors to Ortho Dermatologics. JLS, JW, EAT, JS, and PSY are investigators with Dow Pharmaceutical Science. TL, SH, GM, and RP are employees of Bausch Health.

**BACKGROUND:** Topical corticosteroids (TCS) are the mainstay of psoriasis treatment. Clinical trials have studied twice-daily dosing, and both safety concerns and labeling limit consecutive use to 2 to 4 weeks. Objective: Investigate safety and efficacy of once-daily halobetasol propionate (HP) 0.01% lotion in moderate-to-severe plaque psoriasis.

**METHODS:** Two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies (N=430). Patients randomized (2:1) to HP lotion or vehicle once-daily for 8 weeks, 4-week follow-up. Primary efficacy assessment: treatment success (at least a 2-grade improvement from baseline in Investigator Global Assessment [IGA] score and “clear” or “almost clear”). Additional assessments included improvement in psoriasis signs and symptoms, Body Surface Area (BSA), and a composite score of IGAxBSA. Patients achieving a 50% reduction in IGAxBSA (IGAxBSA-50) were considered to have a clinically meaningful outcome. Safety and treatment emergent adverse events (AEs) evaluated throughout.

**RESULTS:** HP lotion demonstrated statistically significant superiority over vehicle as early as Week 2. By Week 8, 37.5% of patients were treatment successes compared with only 10.0% on vehicle (P<0.001). HP lotion was also superior in reducing psoriasis signs and symptoms, and BSA involvement. Overall there was a 49.4% reduction in mean IGAxBSA composite score by Week 8, and 56.8% of patients achieved IGAxBSA-50, both P<0.001 versus vehicle. There were only 5 treatment-related AEs following the use of HP lotion, the most common being application site dermatitis (0.7%).

**LIMITATIONS:** IGAxBSA evaluations are post hoc.

**CONCLUSIONS:** Halobetasol propionate 0.01% lotion provides significant efficacy over 8 weeks, with good tolerability and safety.

**PA-60: Safety of Hydrogen Peroxide Topical Solution 40% (w/w) in Patients With Skin of Color and Seborrheic Keratoses: Pooled Analysis of Two Phase 3, Randomized, Double-Blind, Vehicle-Controlled, Parallel-Group Studies**

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**BACKGROUND:** A hydrogen peroxide topical solution, 40% (w/w) (HP40) is approved by the US FDA for the treatment of raised seborrheic keratoses (SKs). Limited information is available regarding HP40 treatment in patients with skin of color. We evaluated HP40 safety in a subset of patients with SKs and Fitzpatrick skin type ≥IV.

**METHODS:** In two phase 3, multicenter, randomized, double-blind, vehicle-controlled studies (NCT02667236, NCT02667275), eligible adults with 4 target SKs (≥1 on the face and ≥1 on the trunk or extremities) were randomized to HP40 or vehicle. Safety assessments were treatment-emergent adverse events (TEAEs) and local skin reactions (LSRs). A post hoc, pooled analysis evaluated HP40 safety in patients with a Fitzpatrick skin type of IV, V, or VI who participated in the two vehicle-controlled phase 3 trials.

**RESULTS:** A total of 97 patients with Fitzpatrick skin types of IV, V, or VI were included in the pooled analysis (HP40, n=39; vehicle, n=58). Baseline demographics were similar between groups (mean age, 67.3 years; female, 49.5%). Incidences of LSRs were similar between groups, and most were mild. By visit 8 (day 106, end of study), no HP40-treated patients reported an LSR of
pruritus or stinging and no investigator observed atrophy, edema, erosion, scarring, ulceration, or vesicles. At visit 8, investigator-observed LSRs among HP40-treated target lesions were mild (crusting, 3.8%; erythema, 3.2%; hyperpigmentation, 11.5%; hypopigmentation, 2.6%; scaling, 3.8%) or moderate (crusting, 0.6%; hyperpigmentation, 2.6%). No severe LSRs were reported at visit 8. Only 1 TEAE was reported (post-procedural complication in the HP40 group).

**CONCLUSIONS:** HP40 treatment was safe and well tolerated in patients with skin of color and SKs on the face, extremities, and trunk. At the final study visit (day 106), no LSRs were severe, and all except crusting and hyperpigmentation were mild.

**DISCLOSURES:** Catherine Hren participates in advisory boards for Aclaris Therapeutics. Terry Jones is an investigator for Aclaris Therapeutics. Eduardo Tschen conducted clinical trials for Aclaris Therapeutics. Mark Bradshaw is a statistical consultant to Aclaris and owns stock in that company. Judith Schnyder and Stuart Shanler are employees of Aclaris and may own stock/stock options in that company.

**PA-61: Secukinumab Improves GRAPPA-OMERACT Core Domains of Psoriatic Arthritis**

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**INTRODUCTION:** Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralizes IL-17A, has demonstrated efficacy for patients with psoriatic arthritis (PsA) in multiple phase 3 clinical trials. To improve and standardize the assessment of outcomes, the PsA core domain set has been updated by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and endorsed by Outcome Measures in Rheumatology (OMERACT) in 2016. The updated PsA core domains are: musculoskeletal disease activity (arthritis, enthesisitis, dactylitis, and spine symptoms), skin disease activity (psoriasis and nail psoriasis), pain, patient global assessment, physical function, fatigue, health-related quality of life, and systemic inflammation. Here we report the efficacy of SEC vs placebo (PBO) across individual PsA core domains using pooled data from four phase 3 FUTURE studies.

**METHODS:** Patients with active PsA participated in the phase 3 clinical trials FUTURE 2, 3, 4, and 5 (397, 414, 341, and 996 patients, respectively). Data were pooled into SEC dosed at 150 mg (load vs no load), 300 mg, or PBO at the end of the 16-week double-blind period, and efficacy was evaluated according to the updated GRAPPA-OMERACT PsA core domains. Core domains were assessed using multiple instruments, with improvement defined as percentage of patients achieving ≥50% improvement (joints), complete resolution (arthritis, enthesisitis, dactylitis), or minimal clinically important difference in PsA where known and/or least squares mean change from baseline (patient-reported outcomes). Axial data are from MEASURE 2 (not assessed in future studies).

**RESULTS:** 2049 patients were included; 461 received SEC 300 mg, 572 received SEC 150 mg, 335 received SEC 150 mg no load, and 681 received PBO. Baseline demographics and disease characteristics were broadly similar in all treatment groups. SEC demonstrated significant efficacy vs PBO (P<0.05) across GRAPPA-OMERACT PsA core domains in the phase 3 clinical trials program using multiple instruments and thresholds to measure improvement. SEC 300 mg had the greatest efficacy across domains vs PBO.

**CONCLUSION:** SEC improves both the disease manifestations and life impact of PsA as demonstrated using the PsA core domain set.


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**DISCLOSURE INFORMATION:** AM Orbai: research grant: AbbVie, Eli Lilly, Horizon, Janssen, Novartis; consulting fees or other remuneration: AbbVie, Lilly, Novartis, Pfizer Inc. I McInnes: research grants: Janssen, Celgene, UCB, BMS; consulting fees or other remuneration: Novartis, Janssen, AbbVie, Celgene, Lilly, Pfizer, Leo, UCB, BMS. L Coates: research grant: AbbVie, Celgene, Novartis, Pfizer; consulting fees: AbbVie, Amgen, BMS, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Prothena, Sun Pharma, UCB; speaker’s bureau: AbbVie, Celgene, Janssen, Lilly, Novartis, UCB, ME Husni: research grant: Janssen Research and Development, LLC. D Gladman: research grant: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, Pfizer; consulting fees: AbbVie, Amgen, BMS, Celgene, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB; L Pricop, O Chambenoit, X Meng: stock and employment: Novartis. P Mease: research grant: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN, UCB; consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN, UCB; speaker’s bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, UCB. This investigation was sponsored by Novartis Pharma AG, Basel, Switzerland.
PA-62: Secukinumab Optimized Dosing in Subjects with Moderate to Severe Plaque Psoriasis and PASI ≥75 to <90 Response at Week 24: Results from the OPTIMISE Study

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BACKGROUND: There is an unmet medical need to address the heterogeneity in clinical response to targeted therapies such as secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin-17A. Optimization of the dosing regimen based on individual responses to therapy was investigated in OPTIMISE by evaluating the standard 4-weekly dosing (q4w) vs the 6-weekly (q6w) dosing in the Psoriasis Area Severity Index (PASI) 90 responders and the twice-weekly dosing (q2w) in PASI ≥75 to <90 responders at week 24. This report presents the response achieved at Week 52 by the PASI ≥75 to <90 responders at Week 24 after intensifying therapy through a shortened q2w dosing interval regimen. Analysis of pharmacokinetic (PK) data was also performed for the full treatment period.

METHODS: The OPTIMISE study was a randomized, multicenter, open-label, rater-blinded Phase 3b study. Subjects (1,647) received secukinumab 300 mg at baseline, Weeks 1, 2, 3, and 4, and then q4w to Week 24 (treatment period 1; TP1). At Week 24, PASI 90 responders were randomized to secukinumab 300 mg q4w (n=644) or q6w (n=662) to Week 52 (TP2). PASI ≥75 to <90 responders at Week 24 were randomized to secukinumab 300 mg q4w (n=114) or q2w (n=92) to Week 52.

RESULTS: A PASI ≥75 to <90 response was achieved in 206 (10.5%) subjects at Week 24. The proportion of those patients with PASI 90 response at Week 52 was 10.0% higher in the q2w group (56.5%) vs the q4w group (46.5%). However, the respective odds ratio of 0.62 (95% CI: [0.35, 1.10]) did not reach statistical significance (P=0.1013); therefore, superiority of the q2w over the q4w dosing regimen was not confirmed. At Week 52, mean PASI scores in q2w and q4w groups were 2.2 (±3.1) and 3.6 (±4.5), respectively. There was a significant effect of body weight in the q4w group: 60.7% vs 39.6% of the patients who reached a PASI 90 response were <90 kg vs ≥90 kg, respectively (P=0.0486). In the q2w regimen, heavier patients (>90 kg) responded at higher rates (57.1%) compared to q4w regimen (39.6%); however, the difference was not statistically significant. Pharmacokinetic analysis investigating the relationship between trough concentrations at Week 48 and PASI 90 responder rates with focus on the comparison between q4w vs q2w dosing and body weight categories (<90 kg or ≥90 kg) showed all groups had overlapping drug concentrations. However, a gradual increase in trough concentrations was observed when shifting from q4w to q2w dosing and from subjects ≥90 kg to subjects <90 kg. This observation was clearly reflected in the lower efficacy demonstrated in the q4w, ≥90 kg group.

CONCLUSION: Continued dosing with q4w by Week 52 resulted in PASI 90 response in about half of the PASI ≥75 to <90 responders at Week 24. Subjects with higher body weight may benefit from the q2w dosing regimen; however, further research is warranted.

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DISCLOSURE: K Reich: served as a consultant and/or paid speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly, Forward Pharma, GSK, Janssen-Cilag, Leo Pharma, Medac, MSD, Novartis, Pfizer, Vertex, Takeda, and Xenoprot. L Puig: received honoraria or consultation fees from Abbvie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Gebro, Janssen, Leo-Pharma, Lilly, Merck-Serono, MSD, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB and has participated in speaker’s bureau sponsored by Celgene, Janssen, Lilly, MSD, Novartis, Pfizer. J Szepietowski: investigator for this study and has lectured for Novartis. A Gunstone: investigator for this study. M Rissler, E Pournara, R Orsenigo: employed by Novartis. This investigation was sponsored by Novartis Pharma AG, Basel, Switzerland.

PA-63: Secukinumab Provides Rapid Relief from Pain and Itch in Patients with Moderate-to-Severe Psoriasis: Diary Data from Pooled ERASURE and FIXTURE Studies

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BACKGROUND: Effective treatments for moderate-to-severe psoriasis should relieve psoriasis-related symptoms, eg pain and itch, beyond clearing skin. For many patients, itch is the most bothersome symptom and is closely related to psychosocial well-being. Secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin 17A, is approved for treatment of adult patients with
Secukinumab Shows High and Sustained Efficacy in Subjects with Moderate to Severe Palmoplantar Psoriasis: 2.5-Year Results from the GESTURE Study

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BACKGROUND: Palmoplantar psoriasis (ppPsO) occurs in up to 40% of plaque psoriasis subjects and is often resistant to treatment. It is associated with pain, functional limitations, and greater impairment of health-related quality of life compared with plaque psoriasis on other parts of the body. Secukinumab, a fully human monoclonal antibody, which selectively neutralizes IL-17A, has demonstrated significant efficacy in the treatment of moderate to severe psoriasis and psoriatic arthritis, indicating rapid onset of action, sustained responses, and a favorable safety profile. Here we report the long-term follow-up efficacy and safety results from the GESTURE study, the first robust (2.5-year) data reported in subjects with moderate to severe ppPsO treated with secukinumab.

METHODS: GESTURE is a double-blind, randomized, placebo-controlled, parallel-group, multi-center phase 3b study to investigate safety and efficacy of secukinumab 150 and 300 mg s.c. in 205 subjects with moderate to severe ppPsO treated with secukinumab.

RESULTS: As previously reported, after 16-week placebo-controlled treatment, the primary endpoint palmoplantar Investigator’s Global Assessment (pPGA) 0/1 and all secondary endpoints of this study were met, demonstrating superiority of secukinumab to placebo at Week 16. An interim analysis at Week 80 established the continuation of improvement of palmoplantar disease for all efficacy parameters. The effect was sustained through 2.5 years with 59.2% and 52.5% of subjects in secukinumab 300 and 150 mg groups, respectively (multiple imputation [MI]), achieving clear or almost clear palms and soles (ppIGA 0/1). Consistent with this observation, the mean palmoplantar Psoriasis Area and Severity Index % change from baseline reached −74.7% and −61.6% for secukinumab 300 and 150 mg, respectively, at 2.5 years (MI). The Dermatology Life Quality Index 0/1 response
was achieved in 45.5% vs 23.9% of subjects for secukinumab 300 and 150 mg groups, respectively, (last observation carried forward [LOCF]). Pain and function of palms and soles were markedly improved with secukinumab, as reflected by the Palmoplantar Quality of Life Instrument overall scores with 16.7% and 17.9% subjects experiencing no difficulty in hand and feed functionality in secukinumab 300 mg and 150 mg groups, respectively (LOCF). The safety profile was consistent with that seen in secukinumab phase 3 trials. The most common adverse events across all treatment arms were nasopharyngitis, upper respiratory tract infection, and headache.

CONCLUSION: GESTURE, the largest and longest duration randomized controlled trial to date, revealed that secukinumab provides a novel treatment option for the difficult-to-treat and infrequently studied psرجات ألوان population by providing a strong and sustained response through 2.5 years.

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PA-65: Speed of Onset and Duration of Response Among Ixekizumab-Treated Psoriasis Patients in the Real-World Setting: Results from a Single US Dermatology Referral Practice

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BACKGROUND: Clinical trial data have demonstrated efficacy of ixekizumab for treatment of psoriasis; however, there are limited published data available on its effectiveness in the real-world setting.

OBJECTIVE: The objective of this study was to assess the percentage of patients achieving target disease severity and quality of life (QoL) outcomes at 3-month intervals over the first year of ixekizumab treatment among psoriasis patients at a single US dermatology referral practice.

METHODS: Medical charts of adult psoriasis patients initiating ixekizumab treatment (index) at the referral practice between March 22, 2016 (ixekizumab approval date) and February 28, 2017 were reviewed. Data were collected for the year prior to index and from index until February 28, 2018, or until ixekizumab discontinuation, whichever was first. Summary statistics were generated for patient characteristics and prior treatments received. Static Physician Global Assessments (sPGA) and Dermatology Quality of Life Index (DLQI) were summarized at 1 month post-index and at 3-month intervals pre-and post-index. Additionally, sPGA and DLQI at 12 months were summarized for the subgroup of patients who had achieved an sPGA score of 0 or 1 (sPGA 0,1) by 3 months. Results are presented for patients with data available at each time point (+/- 45 days).

RESULTS: The study cohort included 106 ixekizumab-treated psoriasis patients with mean disease duration of 15 years (median age 47.9 years, 93% Caucasian, 67% male, 95% privately insured). At index, 74% (n=78) of patients had received prior biologic therapy for psoriasis, predominantly with a TNF-α inhibitor (n=47), secukinumab (n=27), and/or ustekinumab (n=12). Approximately half had received prior systemic treatment (52%), such as methotrexate, and/or topical treatment (51%). At index, 8% of patients had sPGA 0,1 (clear or almost clear skin), including 3% with sPGA 0 (clear skin), and 21% had a DLQI score of 0 or 1 (DLQI 0,1). At 1 month post-index (n=95, data available), 59% had sPGA 0,1, including 30% with sPGA 0. At 3 months (n=100), 74% had sPGA 0,1, including 53% with sPGA 0. At 12 months (n=72), 63% had sPGA 0,1, including 39% with sPGA 0. Among the patients with sPGA 0,1 at 3 months (n=74), 67% maintained sPGA 0,1 at 12 months, including 47% with sPGA 0 (n=60, data available). The percentage of all patients with DLQI 0,1 at 1,3, and 12 months post-index were 56%, 67%, and 67%, respectively. Among those patients with sPGA 0,1 at 3 months, 73% had DLQI 0,1 at 12 months. At 12 months, 74% (n=78) of patients in the cohort continued to receive treatment with ixekizumab.

LIMITATIONS: This study was conducted at a single dermatology referral practice in the US. Findings should be confirmed in larger multi-site studies.

CONCLUSION: In this real-world cohort study of ixekizumab-treated psoriasis patients at a US dermatology referral practice, nearly three-quarters of patients had clear or almost clear skin after 3 months of ixekizumab treatment, and over half had clear skin. Among those who had clear or almost clear skin at 3 months, two-thirds of patients maintained that response at 12 months, a higher proportion than among the overall cohort.

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DISCLOSURES: Craig Leonardi has received honoraria from Eli Lilly for the following: Advisory Board, Speaker, Consultant, and has received other financial benefit from Eli Lilly for the following: Investigator. Katherine Osenenko, Solmaz Setayeshgar, and Sisi Wang
are employees of ICON plc., a company contracted by Eli Lilly to conduct this study. David Amato, Mwangi J Murage, Chen-Yen Lin, and William N Malatestinic are employees of Eli Lilly.

**FUNDING:** The study was sponsored by Eli Lilly and Company. Medical writing services were provided by ICON plc, and were funded by Eli Lilly and Company.

**PA-66: The Animal Model of Pre-Incisional N-Acetylcysteine Injection on Surgical Wound Healing – Molecular and Macroscopic Assessment**

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**BACKGROUND:** N-Acetylcysteine (NAC) is a widely used drug. Its antioxidative and mucolytic features found application in pulmonology, radiology, and toxicology. NAC directly reduces the level of reactive oxygen species and increases production of glutathione—an endogenous antioxidant. Both mechanisms may contribute to limit the extent of inflammation that occurs during first steps of wound healing. The main role of the process is to remove dead cells and prevent infections. However, extended inflammation results in impaired wound healing. Thus, reduction of inflammation is demanded. NAC has never been examined as a preinjury, anti-inflammatory agent.

**OBJECTIVES:** The aim of the study was to evaluate the efficiency of NAC enrichment in a local anesthesia administered in case of the surgical incision. Assessment relied on wound healing gene panel expression analysis and macroscopic measurement of wound size over time.

**METHODS:** The study protocol has been approved by I Local Ethics Committee (No. 304/2017). 24 Sprague-Dawley rats were included. Each rat had 6 injections planned on the dorsal side (3 on both sides of the vertebral column). Sides were randomly selected for different agents’ injections—one side received standard lidocaine with epinephrine solution, the other was treated with 3 concentrations (0.015%, 0.03%, and 0.045%) of NAC (Sandoz) dissolved in local anesthetic with epinephrine. Injections of solutions were performed at least 15 min before incisions. 6 rats from each group were sacrificed in 3rd, 7th, 14th, and 60th day after the operation. Photographic documentation of wound healing was performed. Healed wounds were excised and preserved according to further analyses, namely, histologic evaluation (separate study) and gene expression analysis. Gene expression assays included measurement of 94 target genes related to wound healing process with Real-Time PCR technique. Photographic documentation of wounds underwent planimetric analysis with Image J 1.48v to calculate wound area, length, a width within 3 points. Data were verified in terms of its distribution. Mann U Whitney and ANOVA Kruskal-Wallis tests were used.

**RESULTS:** 29 target genes exhibited statistically different expression in both groups. Skin samples treated with any concentration of NAC had higher expression (p<0.05) of growth factors (FGF2, FGF10, IGF2) and selected cytokines (TNF, VEGFB, TGF-α, TGF-b20, IL-10, ELANE), cell adhesion molecules (CDH1, ITA5), and proliferation or remodeling factors (MMP2, CSK, IGF1). However, there was no difference in collagen genes’ expression in both groups (p<0.05). Wound area of a wound from NAC-treated groups was significantly smaller starting from the 28th day after incision, and it lasted to 60th day (p<0.01). A shorter length of wound/scar after NAC administration significantly appeared at the 14th day. Especially beneficial results occurred with 0.030% concentration of NAC in local anesthetic solution.

**LIMITATIONS:** Histological evaluation is still ongoing (Masson’s Trichrome, HE, and IHC stainings) and will provide a full description on the process of healing on each stage confirming or denying findings of molecular and macroscopic analyses.

**CONCLUSIONS:** Results indicate the usefulness of NAC in pre-incisional anesthetic solution. NAC increases the activation of growth factors and cytokines involved in wound healing. Promotes cells’ adhesion molecules and wound bed remodeling. Extended histological analyses will determine precisely the beneficial impact of NAC-induced wound healing. NAC is a safe drug and may be easily transferred into the randomized clinical trial on a human.

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**DISCLOSURES:** All authors have nothing to disclose.

**FUNDING:** This study was partially supported by a statutory research activity grant received from Centre of Postgraduate Medical Education in Warsaw (501-1-06-09-17).

**PA-67: The Hidden Impact of Seborrhoeic Keratoses: Analysis of a Psychometric Survey of an Ethnically Diverse Cohort of US Adults**

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**PURPOSE:** Seborrhoeic keratoses (SKs) are among the most common benign skin lesions, yet individual perception of these lesions is not well understood. A survey was conducted to assess the psychosocial impact of having SKs.
**DESIGN:** An online survey of U.S. consumers was conducted between September 28 and October 13, 2017. Eligible survey participants were aged 35–65 years old and were previously diagnosed with SKs by a healthcare provider (HCP) or self-confirmed the presence of SKs using the definition and example images provided for the survey. Eligible participants must have been bothered by the appearance of SKs located on the face or hairline (score ≥3 on a 5-point Likert scale [1=not at all bothered; 2=slightly bothered; 3= somewhat bothered; 4=moderately bothered; 5=extremely bothered]). The survey had over 80 questions, which included but were not limited to assessments of socio-demographics, participant perceptions, coping behaviors, and experience with HCPs related to their SKs.

**RESULTS:** A total of 702 adults with SKs (mean age, 55 years; female, 80%; mean annual household income, $120,566) completed the survey. Participants were non-Hispanic white/Euro-American (62%), East Asian/Asian American (13%), Hispanic/Latin American (12%), African American (10%), multi-ethnic/racial (3%), or South Asian/Indian American (1%). Among 468 participants (67%) with SKs on multiple body locations, SKs on the face or hairline were of greatest concern (86%). A total of 314 participants (45%) had consulted a professional about their SKs when asked why, the most common reasons given by 208 responders were concern that the lesion could be cancerous (60%) and dislike of how the lesions looked or felt (56%). A majority of survey participants (n=591; 84%) reported attempts to mask or modify their SKs; make-up application was the most common strategy (53%; 65% of females and 8% of males), followed by use of over-the-counter products such as wart removers or anti-aging products (44%), and avoidance of sun exposure (27%). A majority of survey participants (n=569; 81%) were extremely interested or very interested (Likert scale score of 4 or 5) in receiving treatment for their face/hairline SKs (mean score, 4.3). However, a majority of survey participants (n=502; 72%) elected not to have their face/hairline SKs removed. Reasons cited included lack of awareness that treatment options exist (29%) and never being offered the option by their HCPs (19%).

**CONCLUSION:** Individuals with SKs on the face or hairline have concerns about potential skin cancer and/or appearance. Findings from this survey highlight the negative impact benign SKs could have on patients, and inform dermatologists and other HCPs on missed opportunities to improve communications with patients on SK treatment options.

**DISCLOSURES:** Shuai Xu, MD, MSc, reports consulting for Aclaris Therapeutics. He also reports grant support from Pfizer Inc, Leo Pharma, and Novartis. Stacy Wang, PharmD, is an employee of Aclaris Therapeutics, Inc., and Esther Estes, MD, MPH, is a former employee of Aclaris Therapeutics, Inc.

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**PA-68: Withaferin A Loaded PLGA Microparticles as an Advanced Strategy to Treat Scleroderma: Molecular Evidence for Targeted Dermal Drug Delivery**

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**ABSTRACT:** Dermal fibrosis is one of the significant clinical manifestations of scleroderma, hallmarked by excess dermal thickening and aberrant fibrotic events above and beyond other internal organ fibrosis. Scleroderma initiates with inflammation phase and progressively results in thickening and scarring of the dermal tissue due to aberrant occurrence of epithelial to mesenchymal transition and excess extracellular matrix deposition. Unmet clinical need for treatment of dermal fibrosis often makes its management more complicated. Natural compounds have been playing an incredible role to treat various ailments not excluding scleroderma. Towards this context, we previously evaluated the role of Withaferin A (WFA), an active constituent of Withania somnifera as a potent anti-fibrotic agent, in ameliorating dermal fibrosis upon intraperitoneal administration in a 28 day murine experimental model. The objective of the present study was to evaluate the effect of WFA microparticles, as a targeted and sustained drug delivery approach in attenuating Bleomycin induced dermal fibrosis when compared to WFA free drug (2 mg/kg) administered subcutaneously. As per our hypothesis, single dose of WFA microparticles administered via subcutaneous route significantly ameliorated the progression of dermal skin fibrosis compared to unformulated WFA. WFA microparticles exhibited potent EMT inhibition property as evident from the decreased expression of vimentin, α-SMA and restoration of E-cadherin. Significant reduction in dermal thickness, which is a key clinical phenotypic feature of scleroderma, was observed upon treatment with WFA microparticles, which was mirrored through haematoxyline and eosin staining. Further, results of the hydroxyproline assay and Masson’s trichrome staining revealed the role of WFA microparticles in reducing the excess collagen accumulation. Pivotal proteins involved in fibrotic signaling like TGF-β1, Smad2/3, its phosphorylated form, and fibronectin were also significantly attenuated by WFA microparticles, which was apparent from the results of various protein expression studies including western blotting and immunohistochemistry. Briefing the above findings, targeted and sustained release of WFA via microparticle drug delivery system hampered the progression of dermal fibrosis by modulating fibrotic signaling cascades including epithelial to mesenchymal transition and excess extracellular matrix deposition.