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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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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.
MATERIALS/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 posttreatment 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.
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.
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DISCLOSURES: Tina Lin, is an employee of Bausch Health; Leon Kircik: has been a consultant and investigator for Valeant Pharmaceuticals.

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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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.
MATERIALS/METHODS: Multicenter, randomized, double-blind,

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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.

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 two weeks daily-treatment. Both treatments were well-tolerated over the short duration of the study.

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DISCLOSURES: Francisco Kerdel: is an investigator for Valeant Pharmaceuticals. Zoe Draleos: is an investigator for Valeant Pharmaceuticals. Stephen Tyring: is an investigator for Valeant Pharmaceuticals. Tina Lin and Radhakrishnan Pillai are employees of Bausch Health.

PA-03: 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 15000 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).

OBJECTIVE: We recently presented our long-term update on >12000 patient-years (PY) revealing a consistent safety profile over time. Here we summarize integrated safety data based on 15212.5 patient-years of IXE exposure during 12 clinical trials in patients with psoriasis.

MATERIALS/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 patients with 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 15212.5 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 remain 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.

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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DISCLOSURES: Dr. Armstrong is a Board member: Leo Pharma, Novartis, Abbvie, Janssen, Eli Lilly, Ortho Dermatologice Pfizer, Regeneron & Sanofi; Consultant: Leo Pharma, Novartis. Abbvoe. Janssen, Eli Lilly, Modernizing Medicine, Celgene, Ortho Dermatologics, Pfizer, Regeneron & Sanofi, and Science 37; Grants/Grants Pending: Janssen, Abbvie, Eli Lilly; Honoraria: Leo Pharma, Novartis, Abbvie, Janssen, Eli Lilly, Modernizing Medicine, Celgene, Ortho Dermatologics, Pfizer, Regeneron & Sanofi, Science 37; Payment for development of education presentations including speakers service: Abbvie, Janssen, Eli Lilly, Regeneron & Sanofi. Dr. Xu, Dr. Agada, and Dr. Gaia are full time employees and own stock in Eli Lilly and Company.

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PA-04: Analysis of Trends in Invasive Melanoma – Greater Vancouver, Canada

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BACKGROUND: Cutaneous invasive melanoma (IM) accounts for the majority of skin cancer related deaths. Incidence and mortality rates of melanoma have been rising worldwide in recent decades. In 2014, an estimated 76,100 patients were diagnosed with melanoma

and approximately 9710 patients died from melanoma in the United States. Melanoma is associated with the highest cost per death and the highest loss of productive-life years in Europe. The ultimate goal of melanoma prevention is a reduction in incidence and mortality. In recent decades, there has been a global continuous increase within the Caucasian population in both genders. There is a lower incidence of melanoma and higher mortality in males compared to females. Understanding the epidemiologic trends of IM over time will provide important information on primary and secondary prevention.

OBJECTIVE: It is imperative to understand the underlying epidemiology in order to focus efforts on prevention and treatment. We hypothesize that patient demographics and tumour characteristics have changed during the past decades. In order to improve targeted preventative efforts, the main aim of this study is to describe patient demographics and tumour characteristics in a cohort of patients in Greater Vancouver diagnosed with IM. This study aims to compare and analyze the epidemiology of IM in the Greater Vancouver Area over a 13-year period. Data from 2003 is directly compared to that of 2016.

MATERIALS/METHODS: 524 pathology reports were collected through Sunset database, a cancer database, regarding patients diagnosed with either invasive IM or Melanoma in situ (MIS). Data was collected for the years 2003 and 2016, collected from Vancouver-General-Hospital, UBC hospital, Richmond-Hospital, and Lions-Gate-Hospital. The total population of the study consisted of approximately 1 million (15.3% population growth from 2003 to 2016). Patient age, sex, anatomic location, and depth of invasion was recorded. Anatomic localization was categorized into four regions: trunk (abdomen, back, chest), lower limbs (hip, leg, foot, groin), upper limbs (arm, axilla, hand, shoulder), and head and neck (face, neck, scalp) region. The age distribution was categorized into the following categories: under 40, 40-59,60-79, and 80 years or older. Lesions under 0.8mm thick (depth of invasion) were classified as thin melanoma and lesions 0.8mm or greater were classified as thick melanoma based on the updated American Joint Committee on Cancer Staging (AJCC) guidelines.

The two groups of data (2003 and 2016) were compared according to age, gender, localization and depth of invasion. In the case of continuous variables, the Mann-Whitney test was used to determine significant differences. Categorical variables were assessed by the Chi-squared test. Parametric t-tests were used to assess for statistically significant differences in the means and proportions of cases.

RESULTS: In 2003, 68 males were diagnosed with IM, whereas cases increased to 99 males in 2016. With respect to female patients diagnosed with IM, 106 were diagnosed in 2003 and 79 were diagnosed in 2016. Tumor thickness varied between females and males. There was no statistically significant different in tumor thickness between females and males in both years. In 2016, however, males had a higher percentage of thick melanoma compared to females ($p<0.05$). Based on the literature, it has been demonstrated that men are less likely to seek help for their health.

With respect to anatomical distribution, the most common site for males in both years was the trunk. In 2003, the most common female anatomic site was the lower extremity. In 2016, the upper and lower extremities were the most common anatomic sites for females diagnosed with IM. The mean age of diagnosis, for MIS and IM combined, increased by 6.5 years ($p<0.001$). The ratio of IM to MIS remains comparable for both years (1.39:1 in 2003 to 1.31:1 in 2016). During the 13-year period, the number of IM cases increased 27%.

CONCLUSIONS: The anatomic distribution and the prevalence of IM differed with patient age and sex during the years 2003 and 2016. Careful attention to pigmented lesions, especially in older patients in their sixth decade of life, will facilitate prevention efforts. There is a shift in anatomical location in female patients with emerging upper extremity as one of the most common anatomical locations. These results reinforce the need for early detection of melanoma and ongoing patient education about sun safety.

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ACKNOWLEDGMENTS: The population covered by this study is estimated to be one million. The MIS cases were referred to the pathology departments in hospitals from private clinics, dermatologists, plastic surgeons and general physicians. The catchment area of the hospitals is not well delineated; therefore, it is difficult to calculate the exact population in this study.

PA-05: Association of Absenteeism and Presenteeism with Anxiety and Depression in Patients with Moderate to Severe Psoriasis and Improvement after Treatment: Results from the VOYAGE-2 Trial

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BACKGROUND & OBJECTIVES: To evaluate the impact of psoriasis on absenteeism and presenteeism in patients with moderate to severe psoriasis, and changes after treatment in the VOYAGE-2 study through week 48.

METHODS: VOYAGE 2 is a phase 3, randomized, double-blind, placebo/active comparatorcontrolled trial that enrolled patients (n=992) ≥18 years of age with plaque psoriasis for ≥6 months, an Investigator Global Assessment (IGA) score ≥3, a Psoriasis Area and Severity Index
(PASI) score ≥12, and ≥10% body surface area involvement at baseline who were candidates for systemic/phototherapy. Patients were randomized to guselkumab (GUS), placebo (PBO) or adalimumab (ADA) at baseline. Placebo patients crossed over to receive GUS at week 16 and ADA patients crossed over to receive GUS at Week 28 or beyond. Absenteeism was assessed using the Dermatology Life Quality Index (DLQI) work and school domain question: "Over the last week, has your skin prevented you from working or studying? (Yes=3). If No, how much has your skin been a problem at work or

studying? (A lot=2, A little=1, Not at all=0)". Presenteeism was assessed using four domains from the Work Limitation Questionnaire (WLQ): time management, and physical, mental-interpersonal, and output demands. A composite WLQ index score was derived from responses for these domains. Impact of anxiety and depression on productivity was evaluated using the Hospital Anxiety and Depression Scale (HADS) and a logistic regression model was used to adjust for confounding variables.

RESULTS: At baseline, 22.9% of subjects reported that their skin prevented them from working or studying based on their DLQI work and school domain response. Patients with depression or anxiety at baseline were more likely to report that their skin prevented them from working or studying than those without depression (40.2% vs. 16.2%, respectively) or anxiety (35.1% vs. 15.2%, respectively). Similarly, HADS anxiety and depression scores were highly correlated with work productivity based on WLQ responses at baseline (r=0.59 and 0.64, respectively, both
p<0.001). At Week 24, among patients with a DLQI work domain score of 3 at baseline, 82.1% of patients in the GUS group reported a score of 0 (no impact of their skin on work or study at all), compared to 50.0% in ADA group (p<0.001). Similarly, the GUS group achieved a greater mean percentage of improvement from baseline at Week 24 than the ADA group, respectively, in WLQ EADV 2018 time management (41% vs. 37%), and physical (38% vs. 21%), mental-interpersonal (42% vs. 22%) and output demands (40% vs. 16%). Patients without depression or anxiety showed greater improvement in DLQI work and school domain responses than those with depression or anxiety. After adjusting for depression and anxiety, and baseline work and school impairment using the logistic regression model, the odds ratio for GUS patients having no impact of their skin on work and school activity at Week 24 vs ADA patients was 2.9 (1.8-4.5). At Week 48, sustained reduction of impairment in work or school activity, and improvement in WLQ productivity were observed for GUS treated patients. Conclusion: Improvements in absenteeism and presenteeism in patients with moderate to severe psoriasis treated with guselkumab were significantly better compared to patients
treated with adalimumab.

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DISCLOSURES: April Armstrong is an investigator for Janssen Research & Development, LLC. Neither Dr. Armstong nor his institution has received payment for production of this abstract. Peter Foley is an investigator for Janssen Research & Development, LLC. Neither Dr. Foley nor his institution has received payment for production of this abstract. Chenglong Han is an employee of Janssen Research & Development, LLC. Shu Li is an employee of Janssen Research & Development, LLC. Sean McElligott is an employee of Janssen Research & Development, LLC. Erik Muser is an employee of Janssen Research & Development, LLC. Kristian Reich is an investigator for Janssen Research & Development, LLC. Neither Dr. Reich nor his institution has received payment for production of this abstract. Michael Song is an employee of Janssen Research & Development, LLC.

PA-06: Better Skin Clearance is Associated with Improved Quality of Life in Moderate-to-Severe Psoriasis Patients Treated with Tildrakizumab

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BACKGROUND: Tildrakizumab, a high affinity, humanized, IgG1 κ, anti-interleukin–23 monoclonal antibody, has demonstrated efficacy and safety in patients with moderate-to-severe plaque psoriasis in two phase 3, double-blinded, randomized controlled trials (reSURFACE 1: NCT01722331; reSURFACE 2: NCT01729754). The analysis examined the association between quality-of-life improvements and the degree of skin clearance in patients enrolled in the two phase 3 trials and treated with tildrakizumab 100 mg or 200 mg at weeks 0, 4, then every 12 weeks.

MATERIALS/METHODS: Both trials used a three-part design: Part 1 (weeks 0-12) was placebo-controlled; Part 2 (weeks 12-28) re-randomized placebo patients to receive tildrakizumab 100 or 200 mg; Part 3 (weeks 28-64, reSURFACE 1; weeks 28-52, reSURFACE 2) re-randomized patients from the tildrakizumab arms with Psoriasis Area and Severity Index (PASI) response ≥50 at week 28 to receive the same, a higher, or a lower dose of tildrakizumab, or placebo (randomized withdrawal in reSURFACE 1). The Dermatology Life Quality Index (DLQI) questionnaire was administered at weeks 0, 12, 28, 40, and 52. Tildrakizumab-treated patients were pooled from the two trials and classified into 5 mutually exclusive groups based on their week-28 PASI response: PASI <50, PASI 50-74, PASI 75-89, PASI 90-99, and PASI 100. Baseline characteristics, the proportion of patients with DLQI 0/1, and mean DLQI changes from baseline were examined for each PASI response group.

RESULTS: Overall, 575 patients on tildrakizumab 100 mg (male: 69.6%; mean baseline age: 45.6 years) and 581 on tildrakizumab 200 mg (male: 73.0%; mean baseline age: 45.9 years) were included. At week 28, 8.3%, 22.0%, 40.9%, 66.3%, and 86.5% (8.7%, 35.2%, 43.9%, 70.4%, and 85.9%) of patients with PASI <50, 50-74, 75-89, 90-99, and 100 achieved DLQI 0/1 for those on 100 mg (200 mg), respectively. Patients with higher week-28 PASI response also had greater mean DLQI reductions from baseline at week 28 (100 mg: 5.7-13.4; 200 mg: 5.4-12.9). Similar patterns were observed among patients continuously treated with tildrakizumab 100 mg or 200 mg from baseline to week 52, with better PASI-response patients having greater proportions achieving DLQI 0/1 and greater DLQI reductions sustained from week 28 through week 52.

CONCLUSIONS: Tildrakizumab-treated patients with higher levels of PASI response also demonstrated better quality-of-life improvements. Achieving PASI 100 was not necessarily associated with achieving DLQI 0/1, therefore both efficacy and quality-of-life improvements need to be evaluated separately to provide a complete picture of treatment success.

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DISCLOSURES: Drs. Blauvelt, Tyring, Gooderham, Koo, and Reich

are the clinical investigators of the study sponsored by Merck & Co., Inc., and Sun Pharmaceutical Industries, Inc. Drs. Zhao, Lowry, Rozzo and Mendelsohn and Mr. Parno are employees of Sun Pharmaceutical Industries, Inc. Drs. Li, Cichanowitz, and Rosa are employees of Merck & Co., Inc.

PA-07: Brodalumab, a Human Anti-Interleukin-17 Receptor A Monoclonal Antibody, Shows Low Immunogenicity in Patients with Moderate-to-Severe Psoriasis

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BACKGROUND: Brodalumab has demonstrated high efficacy in the treatment of moderate-to-severe plaque psoriasis. Biological therapies sometimes lead to the development of anti-drug antibodies (ADAs), which may affect pharmacokinetics and compromise efficacy and/or safety of the treatment.
OBJECTIVE: To investigate immunogenicity in brodalumab clinical trials.
MATERIALS/METHODS: Immunogenicity data from a 12-week Phase II study and its 352-week open-label extension, and three 52-week Phase III studies (AMAGINE-1, 2 and -3) were included. All studies were placebo-controlled, with ustekinumab as a comparator in AMAGINE-2 and -3. A highly sensitive (15 ng/mL) electrochemiluminescent bridging immunoassay with a drug tolerance threshold of 100.0 µg/mL, defined by a positive-control antibody, was used to detect ADAs. Positive samples were tested for neutralising ADAs using a cell-based assay. In the Phase III studies, samples were tested at weeks 0, 4, 12, 24, 48 and 52.
RESULTS: Steady-state brodalumab serum concentrations were below the drug tolerance threshold in all samples. 122/4461 brodalumab-treated patients (2.7%) were positive for ADAs at any time after receiving brodalumab; 15 (12%) of which were also positive at baseline. The incidence of ADAs was similar across dosing groups (brodalumab 140 mg: 2.2%; brodalumab 210 mg: 1.9%; variable brodalumab dosing: 3.4%; brodalumab 210 mg after ustekinumab: 2.5%). ADAs were transient in 58 patients (1.4%). No patients had neutralising ADAs, including those who received brodalumab 210 mg after ustekinumab (n=564). There was no evidence of altered pharmacokinetics, loss of efficacy, or changes in the safety profile of brodalumab in subjects who tested positive for binding ADAs. No meaningful differences were observed in the incidence of hypersensitivity or injection site reactions for brodalumab compared with placebo or ustekinumab (hypersensitivity events, week 12 – brodalumab 140 mg: n=39/1491, 2.6%; brodalumab 210 mg: n=26/1496, 1.7%; placebo: n=27/879, 3.1%; ustekinumab: n=8/613, 1.3%; injection site reactions, week 12 – brodalumab 140 mg: n=25/1491, 1.7%; brodalumab 210 mg: n=23/1496, 1.5%; placebo: n=11/879, 1.3%; ustekinumab: n=12/613, 2.0%). The most frequent (≥0.3%) injection site reactions across all brodalumab groups (70, 140, 210 and 280 mg; n=3066) were injection site pain (0.7%), erythema (0.5%) and bruising (0.3%).
CONCLUSIONS: In summary, the incidence of brodalumab-specific immunogenicity in patients with moderate-to-severe psoriasis was low and did not appear to compromise the efficacy, pharmacokinetic, or safety profile of brodalumab, including hypersensitivity and injection-site reactions.
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DISCLOSURES: Kristian Reich has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by Dermatologikum Berlin and SCIderm Research Institute, Hamburg, Germany. Mark Lebwohl is an employee of Mount Sinai, which receives research funds from Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, LEO Pharma, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, UCB, Valeant, and ViDac, and is also a consultant for Allergan, Aqua, Arcutis, Boehringer-Ingelheim, LEO Pharma, Menlo, and Promius. Mads Røpke is an employee of LEO Pharma. Monika Rosen is a former employee of LEO Pharma. Klaus Hansen is an employee of LEO Pharma.
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PA-08: Calcipotriene Plus Betamethasone Dipropionate (0.005%/0.064%) Foam Versus Apremilast: Matching-Adjusted Indirect Comparison and US Cost per Responder Analyses

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BACKGROUND: New and effective topical treatments and systemic treatments with improved safety have blurred the distinction among treatment options, particularly for patients who could be considered for either treatment. Hence, a comparison of the relative efficacy and cost of treatment is pertinent.
OBJECTIVE: Bewley et al. conducted a matching-adjusted indirect comparison (MAIC) analysis to compare individual patient data from studies for calcipotriene plus betamethasone dipropionate (0.005%/0.064%) [Cal/BD] foam with aggregated patient characteristics and treatment outcomes from published efficacy assessments of apremilast in adult patients with moderate-to-severe plaque psoriasis. To identify the economic impact of the analysis in the United States (US), a cost per responder analysis was conducted.
MATERIALS/METHODS: Published clinical trials with sufficiently similar populations and outcomes to support indirect comparisons were identified for Cal/BD foam and apremilast. Priority baseline variables for matching included disease severity (Psoriasis Area and Severity Index, PASI, or body surface area, BSA), quality of life, demographics, psoriasis duration, body mass index, and history of topical treatment. MAIC and United States (US) cost per responder analyses were conducted between Cal/BD foam and apremilast.
RESULTS: The UNVEIL trial of apremilast was compared to four pooled trials of Cal/BD foam in terms of baseline variables and efficacy measures. Individual data from 640 of 748 patients in the pooled studies were matched with summary findings from 148 pa-

tients in UNVEIL. After matching, use of Cal/BD foam for 4 weeks in pooled trials produced a statistically greater PASI-75 response (51.1%) than 16 weeks of apremilast in UNVEIL (21.6%; P<0.001). The Physicians' Global Assessment was also higher with 4 weeks of Cal/BD foam treatment in pooled trials (52.7%) than with 16 weeks of apremilast in UNVEIL (30.4%; P<0.001). Using current US cost data and trial dosing, cost per responder (as defined using PASI-75) for Cal/BD foam is $3,770, and is significantly lower than the cost per responder for apremilast ($66,671). Safety and tolerability outcomes were inconsistently defined in the different studies and were not included in the analysis.

CONCLUSIONS: Results in this study demonstrate that Cal/BD foam has significantly lower cost per responder in the US than apremilast in adult patients with moderate plaque psoriasis.

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DISCLOSURES: Dr. Nyeland reports other from LEO Pharma A/S, during the conduct of the study; other from LEO Pharma A/S, outside the submitted work. Dr. Becla reports other from LEO Pharma S/A, during the conduct of the study; other from LEO Pharma S/A, outside the submitted work. Dr. Patel reports other from LEO Pharma Inc., during the conduct of the study; other from LEO Pharma Inc., outside the submitted work. Dr. Veverka reports other from LEO Pharma Inc. during the conduct of the study; other from LEO Pharma Inc., outside the submitted work. Dr. Swensen reports other from LEO Pharma Inc., during the conduct of the study; other from LEO Pharma Inc., outside the submitted work.

ACKNOWLEDGMENTS: Limitations of this analysis include different definitions of efficacy endpoints between comparator trials, differences in patient randomization, unequal treatment periods, and imbalance of sample size between comparators. This study was conducted by LEO Pharma.

PA-09: Comparison of ixekizumab and ustekinumab efficacy in the treatment of nail lesions of patients with moderate-to-severe plaque psoriasis: 52-week data from the IXORA-S trial

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OBJECTIVE: This analysis examined the efficacy of ixekizumab and ustekinumab in the treatment of nail lesions in patients with moderate-to-severe psoriasis over 52 weeks of treatment.

MATERIALS/METHODS: IXORA-S (NCT02561806) was a Phase 3b, multicenter, randomized, double-blind, head-to-head trial in which patients with moderate-to-severe plaque psoriasis were randomized (1:1) to receive either ixekizumab (160-mg starting dose administered as two 80-mg injections, then 80 mg every 2 weeks for 12 weeks followed by 80 mg every 4 weeks; N=136) or ustekinumab (45 mg/90 mg weight-based dosing at Weeks 0, 4, and every 12 weeks thereafter per label; N=166). Nail Psoriasis Severity Index (NAPSI) was used to assess fingernail psoriasis for all patients presenting with nail involvement at baseline (NAPSI>0), and these patients were included in the present analysis. Each fingernail was scored for bed and matrix psoriasis; then scores were added to obtain total NAPSI fingernail scores ranging from 0 (no nail psoriasis) to 80 (severe nail psoriasis). Categorical data at Week 52 were assessed via logistic regression with treatment, weight, and geographic region as factors. As additional analysis, Fisher's exact test was used for comparison. Missing data were imputed using non-responder imputation. Least squares (LS) means (95% confidence interval [CI]) were calculated for NAPSI and treatment groups compared using analysis of covariance with treatment, weight, geographic region, and baseline NAPSI score as factors, and missing data were imputed using modified baseline observation carried forward.

RESULTS: At baseline, 84 (61.8%) patients randomized to ixekizumab and 105 (63.3%) patients randomized to ustekinumab in IXORA-S had nail psoriasis. Mean NAPSI scores at baseline were 28.3 (standard deviation [SD]: 19.9) and 24.8 (SD: 20.0), respectively. Progressive improvement was observed in both groups. Complete resolution of nail psoriasis (NAPSI=0) was seen in a greater percentage of ixekizumab-treated patients compared with ustekinumab-treated patients by Week 16 (31.0% vs 16.2%, p=0.0227) and continued through Week 52 (61.9% vs 28.6%; p<0.0001). After 52 weeks of treatment, average improvement in NAPSI score from baseline was significantly larger in ixekizumab-treated patients (-22.4, 95% CI: -24.8, -20.0) compared with ustekinumab-treated patients (-15.6, 95% CI: -17.8, -13.4) (p<0.0001).

CONCLUSIONS: Even though improvement in nail psoriasis lesions was observed in both treatment groups of IXORA-S, complete resolution of nail psoriasis was seen in significantly greater percentages of patients treated with ixekizumab compared to ustekinumab through 1 year of treatment. Results suggest that ixekizumab may provide significantly greater clearance of nail psoriasis than ustekinumab. Longer periods of observation will be required to determine if nail lesions continue to improve beyond 1 year of treatment.

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PA-10: Disease Severity and Efficacy Insights: Patient-Level Psoriasis Area and Severity Index (PASI) Scores in Tildrakizumab Psoriasis Trials

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BACKGROUND: Tildrakizumab is a high-affinity, anti–interleukin-23p19 antibody that showed efficacy in 2 phase 3 chronic plaque psoriasis studies (reSURFACE 1 [NCT01722331] and 2 [NCT01729754]).1 Some dichotomous efficacy measures, eg, percentages of patients achieving a ≥75% improvement in Psoriasis Area and Severity Index score (PASI 75 response), provide limited efficacy and post-treatment disease severity information at a patient level. Analysis of patient-level PASI data could address these limitations.
OBJECTIVE: To identify potential insights into efficacy assessment and disease severity using a post hoc analysis of pooled patient-level PASI data from the tildrakizumab phase 3 studies.
MATERIALS/METHODS: reSURFACE 1 and 2 methods have been described previously.1 Patients who participated in either tildrakizumab phase 3 study received tildrakizumab 100 mg (n=616) or tildrakizumab 200 mg (n=622) at Week 0 and Week 4, and every 12 weeks thereafter, or placebo (n=309) at Week 0 and Week 4 then tildrakizumab 100 mg or 200 mg at Week 12 and Week 16. PASI score distributions were analyzed using descriptive statistics.
RESULTS: At Week 0, PASI score distributions were skewed; hence, median PASI scores were used in the analyses. Median PASI scores were 18.0 across groups at Week 0 and decreased in both tildrakizumab groups to 11.0 at Week 4 and 3.0 at Week 12 vs 16.0 at Week 4 and 15.5 at Week 12 in the placebo group. By Week 4 (after 1 dose), 55% of patients in both tildrakizumab arms had PASI scores <12 and would no longer meet moderate to severe plaque psoriasis clinical trial entry criteria. The percentage of patients with PASI scores <12 increased during tildrakizumab treatment: 87% at Week 12, 93% at Week 28 (100 mg); 90% at Week 12, 97% at Week 28 (200 mg). At Week 12, 32% (tildrakizumab 100 mg), 29% (tildrakizumab 200 mg), and 2% (placebo) of patients had PASI scores ≤1.0. By Week 28, 48% (tildrakizumab 100 mg) and 52% (tildrakizumab 200 mg) of patients had PASI scores ≤1.0. Median PASI scores at Week 28 were 2.0 (tildrakizumab 100 mg) and 1.0 (tildrakizumab 200 mg).
CONCLUSIONS: These results indicate that PASI scores may provide additional information about disease severity and resolution with treatment that might not otherwise be available using dichotomous PASI assessments. Most tildrakizumab-treated patients had clinical improvement by Week 4, and ≈50% had nominal residual disease (PASI score ≤1.0) by Week 28.
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DISCLOSURES: KG has received research support from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Novartis; and honoraria for consultation from AbbVie, Amgen, Almirall, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Janssen, Leo, Pfizer, UCB. JC has received research/grant support from AbbVie, Amgen, Boehringer Ingelheim, Janssen, Lilly, MC2 Therapeutics, Merck & Co., Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Sun Pharmaceuticals, UCB, Verrica Pharmaceuticals; has served as consultant for AbbVie, Amgen, Celgene, Dermira, Lilly, Novartis, Sun Pharmaceuticals, UCB; has worked on speakers bureau for AbbVie, Janssen, Lilly, Novartis, Regeneron, Sanofi, and UCB. YP has received grant funding and honoraria as an investigator and member of advisory boards from AbbVie, Amgen, and Janssen; received research grants from Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Galderma, GlaxoSmithKline, Eli Lilly, Leo Pharma, MedImmune, Merck, Novartis, Pfizer, UCB Pharma, and Valeant; and received honoraria as a speaker for AbbVie, Janssen, Celgene, Eli Lilly, Leo Pharma, and Novartis.
AMM and SJR are employees of Sun Pharmaceutical Industries, Inc. JP has served as statistical consultant for Sun Pharmaceutical Industries, Inc., and Kyowa Kirin Pharmaceutical Development, Inc. CE has served as a consultant to AbbVie, Eli Lilly, Encore Dermatology, GlaxoSmithKline, Leo Pharma, and Novartis. Study sponsored by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; analyses funded by Sun Pharmaceutical Industries, Inc, Princeton, NJ, USA.
ACKNOWLEDGMENTS: Analyses were presented at the 5th World Psoriasis & Psoriatic Arthritis Conference, June 27–30, 2018, Stockholm, Sweden.

PA-11: 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 (AMAGINE-1/-2/-3) and one phase 2 trial.
MATERIALS/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 pa-

tients 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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PA-12: Drug Survival is Superior Among Patients Treated with Guselkumab Compared to Adalimumab in the VOYAGE 1 Trial

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BACKGROUND: Drug survival, defined as the probability that a pt will remain on a given drug, is an important surrogate for treatment sustainability in chronic diseases such as psoriasis (PsO). Drug survival is often compared between drugs in real-world registries, but can also be applied to randomized clinical trials with active comparator arms.

OBJECTIVE: We aimed to compare drug survival of 2 biologics indicated for moderate-severe psoriasis: the IL-23 blocker guselkumab (GUS) vs the TNF blocker adalimumab (ADA), in the VOYAGE 1 pivotal trial.

METHODS: In this post-hoc analysis, the study population included all pts randomized to GUS (N=329) or ADA (N=334) in VOYAGE 1. Demographic and disease characteristics were very similar between groups. For the primary analysis, Kaplan-Meier (KM) plots using discontinuation for any reason at the endpoint were generated. Drug survival for GUS vs ADA pts was compared at Wk48. Cox modelling was used to estimate the risk of discontinuation (hazard ratio [HR] with 95% confidence interval [CI] and p value) for the ADA arm vs GUS arm. Specific reasons for discontinuation were tabulated through Wk48 and demographic and disease characteristics of pts who discontinued ADA vs GUS were compared. Secondary analyses were performed considering discontinuation due to: (a) worsening PsO or lack of efficacy; or (b) other adverse events, as separate endpoints.

RESULTS: In the primary analysis (discontinuation for any reason), 91.5% (301 of 329) of randomized GUS pts vs 84.4% (282 of 334) of randomized ADA pts remained at Wk48. The difference in drug survival was statistically significant (p = 0.0053). The HR (risk) for discontinuing ADA vs GUS was 1.88 (95% CI = 1.19-2.98, p = 0.0070). Pts who discontinued ADA had a higher median baseline body weight than pts who discontinued GUS (97.7 kg vs 84.9 kg); other demographic and disease characteristics, including age, gender, baseline disease severity, and previous PsO treatments, were similar between the two groups. When considering discontinuation due to lack of efficacy or worsening PsO, drug survival was superior for the GUS arm vs the ADA arm (99.1% vs 94.9%, respectively, p = 0.0017) and risk of discontinuation was higher for pts in the ADA group compared to those in the GUS group (HR 5.71, 95% CI = 1.68-19.5, p = 0.0054). When considering discontinuation due to an adverse event (other than worsening PsO), drug survival was similar for the GUS and ADA arms (97.0% vs 98.2%, respectively, p = 0.2970) and risk of discontinuation for ADA vs GUS pts was similar (HR 0.60, 95% CI = 0.22-1.66, p = 0.3293).

CONCLUSION: Overall, drug survival was superior for the GUS group vs the ADA group at Wk48 in VOYAGE 1. The high rate of drug survival observed for the GUS group was partly driven by higher efficacy with GUS compared with ADA treatment, as shown previously1. Additionally, the tendency of pts with higher body weight to discontinue ADA may reflect its lack or loss of efficacy in this subgroup. Although these findings need to be confirmed in real-word settings, the superior drug survival of GUS vs ADA in the VOYAGE 1 trial is of potential importance to clinical decision making.

REFERENCES: 1Blauvelt A, Papp K, Griffiths C, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol. 2017; 76: 405-417.

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Neither Dr. Griffiths nor his institution has received payment for production of this abstract. Wayne Langholff is an employee of Janssen Research & Development, LLC. Rongnshuang Lin is a consultant for Janssen Research & Development, LLC. David Pariser is an investigator for Janssen Research & Development, LLC. Neither Dr. Pariser nor his institution has received payment for production of this abstract. Yaung-Kaung Shen is an employee of Janssen Research & Devel-

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PA-13: Early Response to Upadacitinib in Moderate-to-Severe Atopic Dermatitis; Results from a Phase 2b Randomized, Placebo-Controlled Trial

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OBJECTIVE: Atopic dermatitis (AD) is a chronic, inflammatory, skin disease characterized by pruritic lesions. Upadacitinib (UPA), a selective JAK-1 inhibitor, is investigated for treatment of patients with AD and other inflammatory diseases. We evaluated early response to UPA treatment from the initial 16-week, double-blind portion of a phase 2b, 88-week, dose-ranging trial.
MATERIALS/METHODS: Adults with moderate-to-severe AD (EASI ≥16, BSA ≥10%, IGA ≥3) not adequately controlled by topical treatment, or for whom topical treatments were not medically advisable, were randomized to once-daily monotherapy with UPA 7.5, 15, or 30 mg, or placebo (pbo). Missing data were handled by last-observation-carried-forward (continuous variables) and non-responder-imputation (categorical variables).
RESULTS: Of the 167 randomized patients; 166 received study drug (42 in each UPA dose-group; 40 in pbo). Mean percent improvement from baseline in EASI score at week 2 was 39.4%/55.9%/59.0% (p<.001/<.001/<.001) for UPA 7.5/15/30 mg groups vs 9.1% in pbo; at week 16 (primary endpoint), 39.4%/61.7%/74.4% (p<.01/<.001/<.001) for UPA vs 23.0% pbo. Mean percent improvement from baseline in weekly average of daily pruritus Numerical Rating Scale (NRS) at week 1 was 19.0%/28.3%/36.2% (p<.001/<.001/<.001) UPA vs –0.8% pbo; at week 16 (secondary endpoint), 39.6%/48.0%/68.9% (p<.01/<.001/<.001) UPA vs 9.7% pbo. Achievement of EASI 75 at week 2 was by 14.3%/26.2%/33.3% (p<.05/<.001/<.001) UPA patients vs 2.4% pbo; at week 16 (secondary endpoint), 28.6%/52.4%/69.0% (p<.05/<.001/<.001) UPA vs 9.8% pbo. Post hoc analysis showed a positive effect on daily pruritus NRS as early as day 2 (mean percent improvement from baseline: 20.8%/19.3%/33.4% for UPA 7.5/15/30 mg vs 1.7% pbo). Using daily assessment, 7.3%/11.8%/28.9% for UPA 7.5/15/30 mg patients vs 2.8% pbo showed improvement ≥4 points in pruritus NRS at day 2. The most common adverse events (AEs), UPA groups vs pbo, were upper respiratory tract infection (16.7%/11.9%/11.9% vs 10.0%) and AD exacerbation (16.7%/7.1%/11.9% vs 7.5%). Serious AEs (n) were atrial fibrillation (1; pbo), appendicitis (1; UPA 15 mg), pericoronitis (1; UPA 7.5 mg), skin infection and AD exacerbation (1; UPA 7.5 mg).
CONCLUSIONS: UPA treatment induced skin improvements as early as the first visit at week 2; improvements in pruritus were recorded as early as day 2. The positive benefit/risk profile of UPA supports proceeding to phase 3 trials in AD.
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L Beck: Received honoraria as a consultant for Boehringer- Ingelheim, Regeneron, Sanofi, GSK, Celgene, AnaptysBio, Novartis, Abbvie, Puricore, Novan, Asana Biosciences and Lilly. Received grants for clinical trials from Regeneron, Abbvie, Pruricore. Has Pfizer and Medtronics stock.
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PA-14: Effect of Tildrakizumab on Personal Relationships in Patients with Moderate-to-Severe Chronic Plaque Psoriasis

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BACKGROUND: The negative impact of psoriasis extends beyond the patient, affecting his/her social interactions and the quality of life of cohabitants. Furthermore, patients with psoriasis often experience sexual difficulties because of their disease. This analysis examined the effect of treatment with tildrakizumab (TIL) on personal relationships of patients with moderate-to-severe chronic plaque psoriasis.
METHODSs: Patients in two phase 3 trials reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754) were randomized to subcutaneous TIL 200 mg, 100 mg, or placebo (PBO) and received treatment at weeks 0 and 4. PBO patients were rerandomized at week 12 to either TIL 200 mg or 100 mg. Etanercept (ETN) 50 mg (semiweekly until week 12 then weekly until week 28) was also a treatment arm in reSURFACE 2. Data on personal relationships were collected at weeks 12 and 28 from the Dermatology Life Quality Index (DLQI) questionnaire question 8 (Q8) "Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives" and question 9 (Q9) "Over the last week, how much has your skin caused any sexual difficulties". Each question was scored on a scale of 0 (not affected at all) to 3 (very much affected). The data were pooled from reSURFACE 1 and 2.
RESULTS: In all, 1,820 patients had DLQI data. All patients reported a negative effect for Q8 and Q9 at baseline. At week 12, the proportion of patients with no negative effect
(score of 0) on personal relationships (Q8 and Q9) was higher for TIL 200 mg, TIL 100 mg, and ETN than for PBO (76%, 72%, and 64% vs. 39%, respectively). A similar trend was observed for individual questions Q8 and Q9. At week 28, more patients on TIL 200 mg and TIL 100 mg reported no negative effect on personal relationships than those on ETN (85% and 77% vs. 66%; respectively). More patients on TIL 200 mg and TIL 100 mg reported no negative effect than those on ETN for Q8 (89% and 81% vs. 70%; respectively) and for Q9 (89% and 84% vs. 75%, respectively).
CONCLUSION: TIL had a beneficial effect on psoriasis-related personal relationship problems and sexual difficulties, compared to placebo and ETN.
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DISCLOSURES: Drs. Papp, Blauvelt, Reich, Gooderham, Tyring, Sinclair, and Thaci are the clinical investigators of the study sponsored by Merck & Co., Inc., and Sun Pharmaceutical Industries, Inc. Drs. Zhao, Lowry, Rozzo and Mendelsohn and Mr. Parno are the employees of Sun Pharmaceutical Industries, Inc. Drs. Li, Cichanowitz, and Rosa are the employees of Merck & Co., Inc.

PA-15: Efficacy and Safety of Risankizumab (RZB) Compared with Adalimumab (ADA) in Patients with Moderate-to-Severe Plaque Psoriasis: Results from the Phase 3 IMMvent Trial

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OBJECTIVE: To investigate the efficacy/safety of RZB vs. originator (ADA) in patients (pts) with moderate-to-severe plaque psoriasis.
MATERIALS/METHODS: In the phase 3 IMMvent(N=605),trial, pts were stratified by weight, prior TNFi-exposure and randomized 1:1 to receive 150mg RZB(N=301, week [wk] 0, 4, 16, and 28) or ADA(N=304, 80mg at wk-0, 40mg every other week [eow] from wk-1). Wk-16 ADA-treated pts achieving PASI 90 response continued on eow ADA, while non-responders (<PASI50) were switched to RZB (wk 16, 20, and 32). ADA-treated pts achieving PASI50-<PASI90 at wk-16 were re-randomized 1:1 to either continue eow ADA (N=56) or switch to RZB (N=53, wk 16, 20, and 32). Co-primary endpoints for Part A were PASI90 and sPGA0/1 at wk-16. Primary endpoint for Part B was PASI90 at wk-44. Ranked secondary endpoints included PASI75 (wk-16) and PASI100 (wk 16 and 44).
RESULTS: Baseline pt demographics and disease characteristics were similar between two treatment arms. All ranked endpoints were achieved (P<0.001). Wk-16, RZB-treated pts achieved significantly higher PASI90 (72.4%) and sPGA0/1 (83.7%) response rates compared with ADA-treated pts (47.4%; 60.2%). PASI100 was achieved by 39.9% and 23.0% of RZB/ ADA-treated pts, respectively. Among ADA-treated pts achieving PASI50- <PASI90 at wk-16, 66.0% of pts switching to RZB achieved PASI90 response at wk-44 compared with 21.4% of pts continuingADA. Furthermore, 39.6% of pts switching to RZB achieved PASI100 versus 7.1% of pts continuing ADA. Treatment-emergent adverse event (TEAE) rates were comparable across treatment groups in two randomized phases.
CONCLUSIONS: RZB treatment showed greater clinical responses vs. ADA in adult pts with moderate-to-severe plaque psoriasis. ADA-treated pts achieving PASI50-<PASI90 at wk-16, switching to RZB resulted in superior efficacy vs. continued ADA treatment. Rates of AEs leading to discontinuation of study drug, serious AEs, and severe AEs were generally low and frequency of AEs remained stable over time. No additional safety concerns were identified in pts who switched from ADA to RZB.
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DISCLOSURES: K Reich has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by Abbvie, Affibody, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Biopepis,

Sanofi, Takeda, UCB, Valeant, and Xenoport. M Gooderham has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, or grants as an investigator from AbbVie, Akros, Amgen, Arcutis, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, GSK, Janssen, Kyowa Hakko Kirin Pharma, Leo Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, Takeda, UCB, and Valeant. D Thaçi has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant from AbbVie, Almirall, Amgen, Bioskin, Boehringer-Ingelheim, Celgene, Dermira, Dignity, Galapagos, GSK, Janssen, Leo, Lilly, Medac, Merck Sharp & Doehme, Morphosys, Novartis, Pfizer, Regeneron/Sanofi, Samsung, Sandoz-Hexal, Sun-Pharma, UCB, and grants from Celgene and Novartis. JJ Crowley has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Janssen, Maruho, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sanofi-Aventis, Sun Pharma and UCB. C Ryan has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Aqua, Dermira, Dr Reddy's, Janssen, Leo, Lilly, Medimetriks, Novartis, Regeneron-Sanofi, UCB, and Xenoport. JG Krueger has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Akros, Amgen, Boehringer Ingelheim, Biogen Idec, BMS, Celgene, Confluence Life Scientific, Dermira, Eli Lilly, EMD Serono, Escalier, Galderma, GLG, GSK, Innovaderm, Janssen Kadmon, Kineta, Kyowa Kirin, Leo Pharma, Merck, Novartis, Paraxel, Pfizer, Provectus, Regeneron, Roche, Sanofi, Serono, Sun Pharma and Vitae. TF Tsai has conducted clinical trials or received honoraria for serving as a consultant for Abbvie, Boehringer Ingelheim, Celgene, Eli-Lilly, Galderma, GSK, Janssen-Cilag, Leo Pharma, Merck-Serono, Novartis International AG, and Pfizer Inc. M Flack is a full-time employee of Boehringer Ingelheim. Y Gu, DA Williams, and EHZ Thompson are full-time employees of AbbVie and may own stock/options. C Paul has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, GSK, Janssen Cilag, LEO Pharma, Lilly, Novartis, Pfizer, Sanofi Regeneron, and UCB.

PA-16: Efficacy of Ixekizumab in Patients Previously Treated with IL-17 Inhibitors

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BACKGROUND: Previous exposure to biologics is thought to potentially impact the efficacy of subsequent biologic therapies.
OBJECTIVE: 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.
MATERIALS/METHODS: In this phase 3b, multicenter, randomized, double-blinded, parallel-group trial (IXORA-P, NCT02513550), patients with moderate-to-severe plaque psoriasis were randomized at a 2:1:1 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 Q4W 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 for patients with or without prior exposure to any biologic therapy and biologics that target the IL-17 pathway with missing data imputed as non-response at Week 52. Dosing regimen interaction with biologic exposure was evaluated using logistic regression.
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 been previously 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 naive 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 naive 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 the efficacy of ixekizumab through 52 weeks of treatment.
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DISCLOSURES: Dr Blauvelt's institution had clinical study funds paid to his institution by Eli Lilly and is a paid consultant and speaker board member of Eli Lilly. Dr. Papp reports grants and personal fees from AbbVie, grants and personal fees from Akros, grants from Allergan, grants and personal fees from Amgen, grants and personal fees from Anacor, grants and personal fees from Arcutis, grants and personal fees from Astellas, personal fees from AstraZeneca, grants and personal fees from Baxalta, personal fees from Baxter, grants and personal fees from Boehringer Ingelheim, grants and personal fees from Bristol-Myers Squibb, personal fees from CanFite, grants and personal fees from Celgene, grants and personal fees from Coherus, grants and personal fees from Dermira, grants and personal fees from Dow Pharma, grants and personal

fees from Eli Lilly, personal fees from Forward Pharma, grants and personal fees from Galderma, grants from Genentech, grants from GSK, grants and personal fees from Janssen, grants and personal fees from Kyowa Hakko Kirin, grants and personal fees from LEO Pharma, grants from MedImmune, personal fees from Meiji Seika Pharma, grants and personal fees from Merck (MSD), grants and personal fees from Merck-Serono, personal fees from Mitsubishi Pharma, grants and personal fees from Novartis, grants and personal fees from Pfizer, grants and personal fees from Regeneron, grants and personal fees from Roche, grants and personal fees from Sanofi/Genzyme, grants and personal fees from Takeda, grants and personal fees from UCB, grants and personal fees from Valeant, outside the submitted work. Dr. Polzer was an employee of Eli Lilly and Company with stock options. Dr. Zhang is an employee of and owns stock options in Eli Lilly. Dr. Sullivan is a consultant and advisory board member for Eli Lilly, Novartis, and Abbvie. Dr. Hong is a consultant for, received honoraria from, received payment for development of education presentations from, and compensation for travel/accommodations from Amgen, Abbvie, Eli Lilly, Janssen, Novartis, GlaxoSmithKline, Sanofi Genzyme, and Celgene.

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PA-17: Efficacy of Tildrakizumab in Patient Subgroups Across a Phase 2b and 2 Phase 3 Trials in Patients with Moderate to Severe Chronic Plaque Psoriasis

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BACKGROUND: Tildrakizumab is a high-affinity, anti–interleukin-23p19 monoclonal antibody that has recently demonstrated efficacy in a phase 2b and 2 phase 3 randomized controlled clinical trials in the treatment of chronic plaque psoriasis.1,2 Understanding potential efficacy differences between patient subgroups may help to identify the most appropriate patients for tildrakizumab treatment.
OBJECTIVES: To evaluate the effects of tildrakizumab in specific subgroups using pooled data from clinical trials.
METHODS: The tildrakizumab phase 2b (P05495 [NCT01225731]) and phase 3 trials (reSURFACE 1 [NCT01722331] and reSURFACE 2 [NCT01729754])1,2 included patients with psoriasis (≥10% body surface area, Physician's Global Assessment score ≥3, and Psoriasis Area and Severity Index [PASI] score ≥12). In the phase 2b study, patients received placebo or tildrakizumab 5, 25, 100, or 200 mg at Weeks 0 and 4 and every 12 weeks thereafter. In reSURFACE 1 and 2, patients received tildrakizumab 100 or 200 mg at Weeks 0 and 4 (Part 1, Weeks 0–12) and every 12 weeks thereafter. Patients randomized to placebo at baseline received the same dosing regimen, beginning at Week 12. This post hoc analysis included all patients from the full analysis set who received tildrakizumab 100 or 200 mg. The following subgroups were analyzed: age (<65, ≥65 years), gender, race (Asian, white, black/African American, other), psoriatic arthritis (yes, no), failure (yes, no) of at least 1 traditional systemic treatment (methotrexate, cyclosporine, or phototherapy), prior biologic use (yes, no), and weight (≤90 kg, >90 kg). The percentages of patients in each subgroup who achieved a ≥75% reduction in PASI score (PASI 75 responders) versus baseline in the tildrakizumab 100- and 200-mg groups were compared with placebotreated patients at Week 12 using nonresponder imputation for missing data.
RESULTS: Among patients randomized in P05495 (N=355), reSURFACE 1 (N=772), and reSURFACE 2 (N=1090), the differences between tildrakizumab- and placebo-treated patients in the percentages of PASI 75 responders at Week 12 were 56.4% and 59.3% for tildrakizumab 100 and 200 mg, respectively. PASI 75 responses were greater in patients with body weight ≤90 kg compared with >90 kg and in those with no psoriatic arthritis. PASI 75 response was greater in patients aged <65 years compared with ≥65 years, but the small numbers in this subgroup limit interpretation. There were no clear or consistent differences in efficacy between the other subgroups, including prior traditional or biologic agent use.
CONCLUSION: Tildrakizumab 100 mg and 200 mg demonstrated clinical improvements after 12 weeks of treatment in patients with chronic plaque psoriasis. Efficacy was consistent across subgroups but was slightly improved in patients with lower body weight and no psoriatic arthritis. Previous biologic use was not associated with a lower response rate.
References: 1. Papp K, et al. Br J Dermatol. 2015;173:930–939. 2. Reich K, et al. Lancet. 2017;390:276–288.
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DISCLOSURES: YP has received grant funding and honoraria as an investigator and member of advisory boards from AbbVie, Amgen, and Janssen; received research grants from Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Galderma, GlaxoSmithKline, Eli Lilly, Leo Pharma, MedImmune, Merck, Novartis, Pfizer, UCB Pharma, and Valeant; and received honoraria as a speaker for AbbVie, Janssen, Celgene, Eli Lilly, Leo Pharma, and Novartis. MR has served as an investigator for Roche, Merck, and Eli Lilly. LR has served as an investigator for Lilly, Janssen, UCB, and Celgene. JW received research grants from AbbVie, Janssen, Celgene, Boehringer-Ingelheim, Merck, Pfizer, Galderma, Biogen, GlaxoSmithKline, Eli Lilly, Novartis, Regeneron, and UCB, and has served as an advisor/speaker for AbbVie, UCB, Janssen, Sanofi, Regeneron, and Novartis. AMM and SJR are employees of Sun Pharmaceutical Industries, Inc. JP has served as statistical consultant for Sun Pharmaceutical Industries, Inc., and Kyowa Kirin Pharmaceutical Development, Inc. PL has served as an investigator for Merck.
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PA-18: Evaluation of the usability and acceptability of a novel, self-injection device for the treatment of moderate-to-severe psoriasis: Results from the Phase III ORION self-dose study

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BACKGROUND/OBJECTIVE: To evaluate the usability and acceptability of a novel, self-injection device in patients (pts) with moderate-severe psoriasis (PsO).
METHODS: ORION is a Phase 3, multicenter, randomized, double-blind, PBO-controlled studyevaluating guselkumab (GUS) administered with a self-injection device that delivers the contents of a pre-filled syringe via a subcutaneous injection. Patients ≥18 years of age with PsO for at least 6 months, an IGA score ≥3, PASI score ≥12, and BSA ≥10%, and who were candidates for, or may have previously received, systemic therapy or phototherapy were eligible for the study. At baseline, 78 pts were randomized to PBO (N=16) at weeks 0, 4, and 12 with crossover to
GUS 100mg at weeks 16, 20, and 28, or GUS (N=62) at weeks0, 4, 12, 20, and 28. Usability at week 0 was assessed using a 3-step Observer Injection Checklist (removal of cap/position of device/completion of injection). Acceptability was assessed using a self-injection assessment
questionnaire (SIAQ) consisting of 6 domains (feelings about injections/self-image/selfconfidence/pain and skin reactions during or after the injection/ease of use of the self-injection device/satisfaction with self-injection) based on a scale of 0=worst to 10=best experience. All 6 domains were rated post-injection at weeks 0, 4, and 12; 3 domains (feeling about self-injections, self-confidence, and satisfaction with self-injection) were also rated pre-injection at week 0. In addition, at week 12, a 3-question self-dose patient questionnaire about speed of injection/handle design of the device/ease of identifying completion of injection was used to assess acceptability.
RESULTS: The proportion of pts with successful, problem-free injections as assessed by the Observer Injection Checklist at week 0 was 98.7 % (77/78 pts), with one GUS-treated pt using the device improperly. For the 3 SIAQ domains assessed at week 0, overall mean scores ranged from 6.59 to 8.23 prior to first injection; scores remained high or increased over time in both groups. In general, SIAQ post-injection domain scores were favorable (overall means ranging from 7.63 to 9.84) and were comparable between GUS vs PBO at all time points through week 12 across all 6 domains. The overall score for pain and skin reactions during or after injection was ≥9.8 from baseline through week 12, indicating no pain or skin reaction at all. Results from the self-dose questionnaire showed that ≥94.7% of pts favorably viewed speed of injection, handle design, and completion of injection.
CONCLUSION: GUS administered with the self-injection device was associated with successful, problem-free injections and favorable acceptability scores suggesting that, pts had a favorable experience and impression of the device.
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DISCLOSURES: Laura Ferris, H Chih-Ho Hong, Wojciech Baran are investigators for Janssen Research & Development, LLC. Elyssa Ott, Gigi Jiang, Chenglong Han are employees of Janssen Research & Development, LLC. Janssen Research & Development, LLC supported this study.

PA-19: Glycemic Index and Acne: A Pilot Study of Twins

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BACKGROUND: Acne vulgaris is an inflammatory skin condition of the pilosebaceus unit and the most prevalent dermatosis. The current models of acne pathophysiology implicate four main components surrounding the pilosebaceous unit: 1) hyperkeratosis, 2) sebum production, 3) Propionibacterium acnes colonization, and 4) inflammation. Recent epidemiologic studies and molecular and biochemical studies also implicate a high glycemic index (GI) and glycemic load (GL), both predominate features of a westernized diet, in the pathogenesis of acne.
OBJECTIVE: We conducted a 24-hour dietary recall to identify correlations and differences between acne severity, GI, GL, and caloric intake between twins with and without acne (inter-twin variability, IV) and differences between individuals in a twinset either with or without acne (intra-twin variability, IaV). We also used a questionnaire to identify different beliefs held by participants about food items and their relation to acne.
METHODS: We surveyed individuals with and without acne (as determined by a board-certified dermatologist) attending two consecutive Twin's Day festivals in Twinsburg, OH. As part of the 24-hour dietary recall, we had participants list the (brand) name and quantity of food consumed as well as location where the food was obtained (e.g. the name of the restaurant). The food items were cross-referenced with the University of Sydney online database and an online calorie tracking application to determine the GI, GL, carbohydrate content and calories consumed. We also surveyed participants with acne about their beliefs involving food and acne, including which foods they believed improved their acne, foods they believed worsened their acne, and, in general, which foods they believe "make acne worse". Only the initial responses of twins who participated both years were used in the final analysis. Demographic analysis was performed using R. P-values were calculated based on t.test for pairwise comparisons or X2 test for multiple categories comparisons. To ensure robustness, linear regression was applied resulting in strong statistical concordance between methods.**RESULTS:** We surveyed 270 individuals (Acne, N = 186; Control, N = 84) during the two consecutive Twin's Day Festivals. Individuals with acne self-reported consuming more servings of carbohydrates (3.58 v. 2.8, p = 0.0054). Furthermore, individuals

with acne were found to have a higher dietary GI than controls (57.64 v. 54.31, p = 0.041). There was also a significant difference between the different grades of acne severity and the belief that animal products (meat and dairy) worsened acne severity (P = 0.048).

LIMITATIONS: Our study relied heavily on participant contribution and reporting of food items and quantity of items consumed. Furthermore, many participants noted they were traveling during the 24-hour period prior to participation and that what they ate may not be consistent with their normal, daily diet.

CONCLUSIONS: Studies have shown that high GI foods that predominate the western diet may contribute to the pathogenesis of acne. In this preliminary study we found a positive correlation between acne and self-reported carbohydrate consumption and daily dietary GI. Our preliminary results were unable to differentiate differences in GL, calories, or grams of carbohydrates consumed between acne and control. This finding is consistent with previous studies that implicate a high GI diet in acne pathogenesis, possibly through elevated concentrations of serum insulin, IGF-1, and mTORC1. We plan to return to the next Annual Twin's Day Festival in August 2018 to recruit additional participants to further elucidate the correlations between diet and the pathogenesis of acne. While the role of diet in the pathogenesis of acne continues to be expounded upon, general practice should include patient education on healthy eating habits, especially those that overlap with existing knowledge on diet and acne.

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PA-20: Halobetasol and Tazarotene: Further Defining the Role of a Unique Fixed Combination Topical Lotion in Moderate-to-Severe Plaque Psoriasis

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BACKGROUND: A unique fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) lotion has been shown to be effective in psoriasis using Investigator Global Assessment (IGA) tools to assess erythema, plaque elevation and scaling. However, these do not consider changes in Body Surface Area (BSA). The IGAxBSA composite tool is a simple, effective, validated alternative for measuring improvement in psoriasis severity. It correlates well with the Psoriasis Area and Severity Index (PASI) and demonstrates sensitivity to changes from baseline in patients with both mild and moderately severe disease.

OBJECTIVE: To further define the role of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) lotion in moderate-to-severe plaque psoriasis using the IGAxBSA composite tool.

MATERIALS/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 posttreatment follow-up. Efficacy assessments using the validated IGAxBSA composite tool.

RESULTS: HP/TAZ lotion demonstrated statistically significant superiority at Week 8 (versus TAZ and vehicle) and Week 12 (versus HP, TAZ and vehicle). By Week 8, HP/TAZ lotion achieved a 63.5% reduction in mean IGAxBSA composite score compared with 49.2%, 15.2% and 11.9% for HP, TAZ and vehicle (P<.001 versus TAZ and vehicle), that was sustained four weeks posttreatment (P<.001 versus TAZ and vehicle and P=.003 versus HP). A 25% and 50% improvement in IGAxBSA was achieved within 1.9 and 4.6 weeks respectively, and 47.5% of patients achieved IGAxBSA-75 by Week 8, compared with 38.1%, 11.9% and 12.9% with HP, TAZ and vehicle (P<.001 versus TAZ and vehicle).

CONCLUSIONS: HP/TAZ lotion was associated with significant and rapid reductions in disease severity as assessed by the IGAxBSA composite tool. The addition of tazarotene affords sustained benefits posttreatment.

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DISCLOSURES: Linda Stein Gold: is and advisor, consultant, and speaker for Valeant Pharmaceuticals. Jerry Bagel: no relevant conflicts. Mark Lebwohl: is an employee of Mount Sinai which receives research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen / Johnson & Johnson, Leo Pharmaceutucals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, UCB, Valeant, and ViDac. Dr. Lebwohl is also a consultant for Allergan, Aqua, Arcutis, Boehringer-Ingelheim, LEO Pharma, Menlo, and Promius. Tina Lin, Gina Martin, Radhakrishnan Pillai, are all employees of Bausch Health.

PA-21: Impact of Secukinumab on Patient Reported Outcomes in Patients with Psoriasis in Challenging-to-Treat Areas: Real World Data from the Corrona Psoriasis Registry

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BACKGROUND: Psoriasis involving the scalp, nail, and palmoplantar areas is considered challenging-to-treat (CTT) and is associated with substantial physical discomfort, disability, and decreased quality of life. Secukinumab, a fully human anti-interleukin 17A monoclonal antibody, has shown efficacy in improving clinical outcomes in patients with psoriasis in CTT areas. However, no real-world observational studies have evaluated the effect of secukinumab on changes in patient-reported outcomes (PROs) in patients with CTT areas.

OBJECTIVE: To determine the impact of secukinumab on PROs at 6 months among patients with nail, scalp, or palmoplantar psoriasis who initiated secukinumab at enrollment in the US-based Corrona® Psoriasis Registry, a prospective, observational registry.

MATERIALS/METHODS: This study included patients enrolled in

the Corrona Psoriasis Registry from April 15, 2015, through May 10, 2018, who were aged ≥ 18 years, diagnosed with psoriasis localized to ≥ 1 CTT area (nail, scalp, or palmoplantar) by a dermatologist, initiated secukinumab at the time of enrollment (baseline), and had a 6-month follow-up visit (window of 5-9 months) without treatment discontinuation. Patient demographics, clinical characteristics, and treatment history were assessed at registry enrollment. PROs were assessed at baseline and at 6 months and included fatigue (visual analog scale [VAS] 0-100), itch (VAS 0-100), pain (VAS 0-100), Dermatology Quality of Life Index (DLQI; 0-30), and Work Productivity and Activity Impairment (WPAI) questionnaire. Paired t-tests were used to evaluate mean changes from baseline to 6 months in continuous PROs and generalized McNemar tests were used to evaluate changes from baseline to 6 months in proportions for categorical PROs.

RESULTS: A total of 192 patients initiated secukinumab and had psoriasis in ≥ 1 CTT area at registry enrollment, of whom 80 completed a 6-month follow-up visit. The 68 patients (85%) who were still receiving secukinumab at the 6-month visit were included in the analysis. Among these patients, 61 (89.7%) had scalp psoriasis, 28 (41.2%) had nail psoriasis, and 11 (16.2%) had palmoplantar psoriasis. The mean (SD) age at enrollment was 51.2 (14.8) years; 51.5% of patients were female and 79.4% were white. Patients had a mean (SD) psoriasis duration of 21.8 (15.8) years, the majority (89.7%) were biologic experienced, and nearly half (48.5%) had psoriatic arthritis. Patients reported statistically significant improvements at 6 months vs baseline in fatigue (mean [SD], 23.2 [26.6] vs 33.2 [27.3]; P = 0.0100), itch (20.9 [27.3] vs 49.6 [32.5]; P < 0.0001), pain (12.1 [18.3] vs 33.8 [32.0]; P < 0.0001), and DLQI (2.9 [3.9] vs 8.1 [6.1]; P < 0.0001). The proportion of patients indicating that psoriasis had at least a "moderate" effect on life was lower at 6 months than at baseline (22.1% vs 59.7%, P < 0.0001). With respect to the WPAI, patients reported statistically significant improvement at 6 months vs baseline in percent of daily activities impaired (mean [SD], 9.5% [17.7%] vs 17.5% [25.4%]; P = 0.0075). Additionally, the 42 patients who were currently employed reported statistically significant improvement at 6 months vs baseline in percent impairment while working (mean [SD], 3.7% [7.8%] vs 11.2% [19.7%]; P = 0.0148), and there was suggested improvement in overall percent of work hours affected (mean [SD], 4.9% [10.0%] vs 11.9% [20.6%]; P = 0.0486).

CONCLUSIONS: Secukinumab treatment significantly improved fatigue, itch, pain, and quality of life measures at 6 months in patients with psoriasis in CTT areas in this real-world, observational study. These results are consistent with previous reports from secukinumab clinical trials; however, additional real-world studies are needed to evaluate the long-term effectiveness of secukinumab for improving PROs in patients with psoriasis in CTT areas.

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DISCLOSURES: J. Bagel has served as an investigator and consultant for AbbVie, Amgen, Boehringer Ingelheim, Sun, Janssen, Leo, Novartis, Celgene, and Eli Lilly; served as a consultant and speaker for Valiant; and served on the speaker's bureau for AbbVie, Eli Lilly, Janssen, Leo, and Novartis. R. R. McLean, H. J. Litman, and A. Schrader are employees of Corrona, LLC. A. Guana and R. Germino are employees of Novartis Pharmaceuticals Corporation. A. Guzman has nothing to declare. Corrona, LLC, has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Roche, UCB, and Valeant. The design and conduct of the study was a collaborative effort between Corrona and Novartis, and financial support for the study was provided by Novartis. Novartis participated in the interpretation of data and review and approval of the abstract.

ACKNOWLEDGMENTS: Patients in the Corrona Psoriasis Registry are routinely seen and treated by dermatologists voluntarily participating in the registry and therefore may not be representative of all patients with psoriasis in the United States. The sensitivity of some PRO measures depends on the precise localization of psoriasis. The limited sample size precluded comparisons among individual CTT areas.

PA-22: Increasing Incidence of Melanoma in Situ (MIS) in Greater Vancouver, Canada — A Retrospective Cross Sectional Study

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BACKGROUND: In situ melanomas are characterized by malignant melanocytes limited to the epidermis during a non-invasive radial growth phase. Melanoma in situ (MIS) is believed to be a biologic precursor to invasive melanomas. However, not all MIS lesions progress to invasive melanoma (IM). Multiple epidemiologic studies have shown that the incidence of MIS is increasing at a faster rate compared to IM. Understanding the epidemiologic trends of MIS over time will provide important information about primary and secondary prevention of IM. There are few epidemiologic studies looking at clinical features of MIS. This is partially because epidemiologic studies on melanoma have been primarily supported by national registries lacking epidemiologic data about MIS.

OBJECTIVE: It is imperative to understand the underlying epidemiology in order to focus efforts on prevention and treatment. We hypothesize that patient demographics and tumour characteristics may have changed during the past decades. In order to improve targeted examination and intervention, the main aim of this study is to describe patient demographics and tumour characteristics in a cohort of patients from Greater Vancouver diagnosed with MIS. This study aims to compare and analyze the epidemiology of MIS in the Greater Vancouver Area over a 13-year period. In other words, data is compared between 2003 and 2016.

MATERIALS/METHODS: This study consists of 524 pathology reports, which were compiled through the Sunset database. Patients regarding diagnosed with either invasive MM or MIS were included. These reports were collected from 2003 and 2016, respectively from Vancouver-General-Hospital, UBC-hospital, Richmond-Hospital, and Lions-Gate-Hospital. The total population was approximately 1 million (15.3% growth from 2003 to 2016). Patient age, sex, anatomic location, was recorded. We categorized anatomic locations into four regions: trunk (abdomen, back, chest), lower limbs (hip, leg, foot, groin), upper limbs (arm, axilla, hand, shoulder), and head and neck (face, neck, scalp). Ages were categorized into four groups: under 40,

40-59, 60-79 and 80 years and over. The two years (2003 and 2016) were compared according to age, gender, and localization. In cases of continuous variables, the Mann-Whitney test was used to determine significant differences. Categorical variables were checked by the Chi-squared test. The Parametric t-test was applied to assess for statistically significant differences in the means and proportions of cases.
RESULTS: 46 males were diagnosed with MIS in 2003, whereas 70 males were diagnosed with MIS in 2016. 4 females were diagnosed with MIS in 2003, and 64 females were diagnosed in 2016. For female patients, the proportion of IM cases decreased, while the proportion of MIS cases increased. As studies have shown, this could be due to females showing greater concern over aging or damaged skin. The ratio of IM to MIS was 1.39:1 and 1.31:1 in 2003 and 2016, respectively, yielding no statistically significant difference. The patient age at time of diagnosis was 60.4 in 2003, and 66.6 in 2016, and this difference was statistically significant (P<0.001). The mean age of diagnosis therefore increased by 6.2 years (p<0.001). MIS on the trunk in males decreased (52% to 18% of cases) (P<0.001). MIS on the head in males increased (26% to 42% of cases), and the number of MIS cases increased 36%.
CONCLUSIONS: The anatomical distribution of MIS differed with patient age and sex during the period from 2003 to 2016. Overall, the proportion of MIS cases increased while cases of IM decreased. The anatomical distribution of MIS was different in comparison to IM. Careful attention to pigmented lesions in older patients, especially to the head and neck will facilitate earlier diagnosis of MIS. These results reinforce the need for early detection of melanoma and ongoing patient education about sun safety.
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DISCLOSURES: I certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on me (or any other authors) or on any organization with which I (or any other authors) am associated. The authors have nothing to disclose
ACKNOWLEDGMENTS: The population covered by this study is estimated to be one million. The MIS cases were referred to the pathology departments in hospitals from private clinics, dermatologists, plastic surgeons and general physicians. The catchment area of the hospitals is not well delineated; therefore, it is difficult to calculate the exact population in this study.

PA-23: 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.
OBJECTIVE: 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: 14.8, 26.8) 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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DISCLOSURES: AG: Consulting/Advisory Board Agreements/or speakers Bureau for Janssen, Celgene, Bristol Myers Squibb, Beirsdorf, Abbvie, UCB, Novartis, Incyte, Lilly, Reddy Labs, Valeant, Dermira, Allergan, Sun Pharmaceutical Industries; and has Research/Education Grants from Janssen, Incyte, UCB, Novartis, and Lilly. YR's institution consults for Eli Lilly, Novartis, Pfizer, AbbVie, Janssen and Taro; speakers' bureaus for Eli Lilly, Novartis, Janssen; received compensation for expenses from Novartis, AbbVie, and Janssen; outside the submitted work. DS has nothing to disclose. AS, MD, SW are employees of and own stock in Eli Lilly.
FUNDING: This study was sponsored and funded by Eli Lilly and Company and INC Research.

PA-24: Insights into Psoriasis Disease Severity and Treatment Efficacy Using Patient-Level Psoriasis Area and Severity Index (PASI) Scores From Tildrakizumab Phase 3 Clinical Trials

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BACKGROUND: Tildrakizumab, a high-affinity anti-interleukin-23p19 antibody, has demonstrated efficacy in patients with chronic plaque psoriasis.1 Typical psoriasis clinical trial efficacy endpoints, such as ≥90% improvement in Psoriasis Area and Severity Index (PASI 90) response, provide little information on disease severity and are less relevant clinical outcomes than reaching low PASI scores.

OBJECTIVE: We performed a post hoc analysis of pooled data from 2 tildrakizumab phase 3 trials to ascertain the value of patient-level PASI scores and binary PASI improvement measures in understanding clinical trial efficacy results.

MATERIALS/METHODS: In reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754),1 patients received tildrakizumab 100 mg (N=616) or 200 mg (N=622) at Week (W)0, W4, and then every 12 weeks or placebo (N=309) at W0 and W4, followed by rerandomization at W12 and treatment with tildrakizumab 100 or 200 mg at W12 and W16. PASI score distributions were compared using a 2-sample asymptotic Kolmogorov–Smirnov (KS) test of observed data at W0, W4, W12, and W28.

RESULTS: At W0, median PASI score was 18.0 across treatment groups, indicating that a PASI score ≤1.8 was needed to achieve a PASI 90 response in half of the patients. Differences in PASI score distributions between tildrakizumab and placebo arms were significant at W4, W8, and W12 (all KS test P<0.001). At W4 (after 1 tildrakizumab dose), median PASI scores had decreased to 11.0 in both tildrakizumab groups, and PASI scores were significantly correlated with percentage PASI changes (Pearson correlation coefficient r=0.75 and 0.70 with tildrakizumab 100 and 200 mg, respectively; P<0.0001). At W12 (after 2 tildrakizumab doses), median PASI scores had further decreased to 3.0 in both tildrakizumab groups; PASI scores ≤1.0 and ≤2.0, typically representing nominal disease, were achieved by 32% and 46% of patients in the tildrakizumab 100-mg group and by 29% and 47% of patients in the tildrakizumab 200-mg group, respectively. In contrast, PASI 90 response rates at W12 were 38% with tildrakizumab 100 mg and 37% with tildrakizumab 200 mg. At W28 (12 weeks following a third dose), median PASI scores were 2.0 with tildrakizumab 100 mg and 1.0 with tildrakizumab 200 mg; PASI scores ≤1.0 and ≤2.0 were achieved by 48% and 60% of patients in the tildrakizumab 100-mg group and by 52% and 65% of patients in the tildrakizumab 200-mg group. In contrast, PASI 90 was achieved by 54% and 58% of patients in the tildrakizumab 100-mg and 200-mg groups, respectively.

CONCLUSIONS: PASI scoring is poor at distinguishing minimal disease severity. PASI scores of ≤1.0 vs 1.0–2.0 are often clinically indistinguishable and affected by minor variability in physician assessments. Achieving a PASI 90 response required a PASI score ≤1.8 for half of the patients based on median baseline PASI scores; yet, at W12 and W28, 6%–10% more patients had a PASI score ≤2.0 than had a PASI 90 response. These results suggest that absolute PASI scores may provide a more clinically meaningful measure of treatment benefit than PASI 90 response rates, which depend on initial disease severity.

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PA-25: 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).

MATERIALS/METHODS: Patients 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]) 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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ACKNOWLEDGMENTS: 2259 characters (for abstract body including spaces; no limits specified; abstract must include the following information: Background, Objectives, Methods, Results, Limitations [if any], Conclusion, Corresponding Author with contact information, Author

PA-26: Isotretinoin, Creatine Kinase: Conundrum or Laboratory Cacophony

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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 correlate with damage to tissue or intrinsic muscle pathology that result 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.

OBJECTIVE: 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 = 51). We excluded patients that did not have their serum CK evaluated during therapy (N = 9), or lacked a baseline CK evaluation (n = 13). In total 43 patients were part of the analysis (Male, N = 24; Female, N = 19). 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 involvement in high-intensity varsity sport (i.e. 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: Only 2 patients had serum CK > 900 U/L and both were active males. Two individuals who had concurrent exercise also reported transient excessive muscle soreness; no muscle soreness was reported in the group that did not exercise. Patients who exercised had a higher average CK on OI than their sedentary counterparts ($p = 0.039$). Elevated CK was positively correlated with recent exercise ($P < 0.001$). Activity trends were maintained when categorized by gender (for males $P = 0.047$, females $P = <0.001$). There is a slight positive correlation between CK and cumulative OI dose ($R2 = 0.0956$)

LIMITATIONS: Analysis of our chart review was limited primarily by small sample size (N = 43). 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 results are consistent with the current body of evidence, showing males who exercise have a higher CK than their female counterparts and that exercise is capable of raising CK. These initial results highlight concerns that males on OI who engage in exercise have the potential to have the highest CK values and the greatest risk of developing rhabdomyolysis, and 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.

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PA-27: Ixekizumab Provides Rapid and Greater Improvement of the Symptoms of Genital Psoriasis Compared to Placebo in a Randomized, Double-Blind, Phase 3b Clinical Trial

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BACKGROUND: Genital psoriasis (GP) is a common manifestation of psoriasis characterized by pruritus, pain, and other symptoms contributing to sexual impairment and reduced quality of life.

OBJECTIVE: The objective of the study was to evaluate the impact of ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, compared to placebo (PBO) on symptoms of GP during 12 weeks of treatment.

MATERIALS/METHODS: Patients (N=149) with moderate-to-severe GP were randomized (1:1) to receive PBO or 80 mg IXE every 2 weeks following an initial dose of PBO or 160 mg IXE, respectively. Symptoms of GP were measured using the patient-reported

Genital Psoriasis Symptom Scale (GPSS), composed of numeric rating scales (NRS) ranging from 0 to 10 (0=no symptom, 10=worst imaginable) for 8 common symptoms of GP (itch, pain, discomfort, stinging, burning, redness, scaling, and cracking). For GPSS item and total scores, treatment group comparisons were made using a mixed models for repeated measures analysis. For patients with a baseline score of ≥3 in the genital itch NRS, the percentage of patients achieving a ≥3-point improvement from baseline was analyzed using logistic regression analysis and non-responder imputation.

RESULTS: IXE treatment led to a significant improvement ($p<0.001$) in GPSS total score versus PBO within 1 week and through week 12; least square mean (LSM) ± standard error (SE) change from baseline was -31.57 (±2.07) for IXE versus -2.82 (±2.19) for PBO at week 12. IXE was superior to PBO for all individual GPSS items at week 1 ($p<0.01$ for itch, stinging, redness, and scaling; $p<0.001$ for pain, discomfort, burning, and cracking) and week 12 ($p<0.001$ for each item). LSM (±SE) change from baseline for each GPSS item at week 12 (IXE and PBO, respectively) were itch: -4.02 (±0.27) and -0.21 (±0.29), pain: -3.84 (±0.28) and -0.34 (±0.29), discomfort: -4.27 (±0.28) and -0.42 (±0.30), stinging: -3.74 (±0.28) and -0.51 (±0.30), burning: -3.73 (±0.27) and -0.53 (±0.29), redness: -4.45 (±0.27) and -0.63 (±0.29), scaling: -3.80 (±0.26) and -0.02 (±0.27), and cracking: -3.74 (±0.26) and -0.19 (±0.28). Response rates for genital itch NRS ≥3-point improvement were significantly greater with IXE as early as week 2 ($p<0.001$) and through week 12 (IXE: 59.7%, PBO: 8.3%; $p<0.001$).

CONCLUSIONS: During 12 weeks of treatment, patients receiving IXE showed rapid and significantly greater improvements in the severity of GP symptoms versus PBO.

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PA-28: 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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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 a 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.

MATERIALS/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 ³1-grade improvement in baseline IGA were subsequently managed 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.

CONCLUSIONS: HP/TAZ lotion provides rapid and sustained treatment success in patientts with moderate-to-severe psoriasis when followed for 1 year.

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DISCLOSURES: Paul Yamauchi: has served as an investigator for Amgen, Celgene, Dermira, Galderma, Janssen, LEO Pharma, Eli Lilly, MedImmune, Novartis, Pfizer, Regeneron, and Sandoz; he serves as an advisor and/or speaker for AbbVie, Amgen, Baxter, Celgene, Dermira, Galderma, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, and Regeneron. Jonathan Weiss: is an advisor and consultant for Valeant Pharmaceuticals. Tina Lin, Radhakrishnan Pillai, are employees of Bausch Health.

PA-29: Long-Term Real-World Safety and Effectiveness of Adalimumab for Moderate to Severe Psoriasis: Results from the Nine-Year Interim Analysis of the ESPRIT Registry

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BACKGROUND: ESPRIT is a 10-year international prospective observational registry evaluating long-term safety/effectiveness of originator adalimumab (ADA) in adults with moderate-to-severe chronic plaque psoriasis. We report interim analyses over registry's initial 9 yrs.
MATERIALS/METHODS: Enrolled patients (pts) were continuing ADA treatment from a current prescription or previous study participation and received at least 1 ADA dose (All-Treated Population [All-Rx]. Patients were evaluated at 3/ 6 months post enrollment, and every 6 months up to 10 yrs. Data were collected 26 September 2008 through 30 November 2017. Incidence rates (IR) for all treatment-emergent adverse events (All-TEAEs) occurring from the initial dose through 70 days after last ADA dose (excluding AEs during treatment interruptions) are reported as events per 100 patient years of total ADA exposure (E/100PY), including pre-registry exposure. Effectiveness was evaluated by Physician's Global Assessment (PGA), as-observed.
RESULTS: 6016 All-Rx pts (58% male; mean age: 47 yrs; mean weight: 90 kg) were enrolled and dosed. Median duration of total ADA exposure was 1633 days (range 14–5526). Registry discontinuation was 44.0%; the most frequent reason for discontinuing was lost to follow up (19.5%). IR (E/100PY) for All-TEAEs (All-Rx) was: overall 22.1; serious AEs 4.6; malignancies 1.2, lymphoma <0.1, non-melanoma skin cancer 0.7; serious infections (SI) 1.0, active TB <0.1; congestive heart failure <0.1; lupus-like reactions and systemic lupus <0.1; and demyelinating disorder <0.1. IR for All-TEAEs (All-Rx) leading to death was 0.2 E/100PY. Standardized mortality ratio (All-Rx) was 0.35 (95% CI, 0.26, 0.46), indicating that the observed number of deaths was below expected in an age-, sex- and country-matched population. All-Rx pts achieving PGA 'clear' or 'minimal' at 12, 24, 36, 48, 60, 72, 84, 96, and 108 months in the registry were 2629/4614 (57.0%), 2373/4042 (58.7%), 2090/3535 (59.1%), 2034/3243 (62.7%), 1836/2965 (61.9%), 1420/2238 (63.4%), 1051/1595 (65.9%), 423/635 (66.6%), and 15/25 (60%), respectively.
CONCLUSIONS: No new safety signals were observed with ADA treatment during this 9-yr interim analysis and safety was consistent with the known safety profile of ADA. IR of SI and malignancies remained stable with up to >9 yrs of overall exposure to ADA. TE deaths in the registry were below the expected rate compared with the general population. As-observed effectiveness of ADA remained stable through 108 months.
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DISCLOSURES: D Thaçi has received honoraria from AbbVie, Almirall, Amgen, Boehringer, BMS, Celgene, Dignity, Galapagos, Janssen, Leo, Lilly, MSD, Morphosys, Novartis, Pfizer, Regeneron/Sanofi and UCB for participation on ad boards, as a speaker and for consultancy; and received research grants from Novartis and Celgene. 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 Boehringer 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. JJ Wu has received research funding from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, and Regeneron. W Abramovits has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Allergan, Amgen, Anacor Pharm, Aqua Pharma, Celgene, Centocor, Conversant, Eli Lilly, Exeltis, Galderma, Genentech, Glenmark, GSK, Innocutis, Janssen Biotech, Leo Pharma, MediMetricks, Merck Serono, Novartis, Novan, Otsuka, PharmaDerm, Perrigo, Pfizer, Promius, Prothena, PuraCap, Quinnova, Ranbaxy, Regeneron , Sanofi, Taro, Teva, Tioga, Tolmar, Valeant, and Xenoport. 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. D Arikan, D Guo, H Kupper, M Bereswill, and WC Valdecantos are full-time employees of AbbVie and may own stock/options.

PA-30: Long-Term Safety of a Fixed Combination Halobetasol Propionate 0.01% and Tazarotene 0.045% (HP/TAZ) Lotion in Moderate-to-Severe Plaque Psoriasis

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BACKGROUND: A novel halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion formulation has been shown to provide synergistic and sustained efficacy over the individual active ingredients following 8 weeks daily use and 4-week posttreatment follow-up, with good tolerability.
OBJECTIVE: To study the long-term safety and tolerability of HP/TAZ lotion in moderate-to-severe plaque psoriasis
MATERIALS/METHODS: Phase 3 multicenter, open-label study in 555 patients treated with HP/TAZ lotion followed for up to 1 year. Patients 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 were not treatment successes at Week 8 were to be treated for a further 4 weeks; otherwise they received no further treatment at this time. All patients were evaluated at Week 12; those demonstrating ³1-grade improvement in IGA from baseline continued in the study. Treatment continued in four-week cycles: either HP/TAZ lotion once-daily for 4 weeks if they had not achieved treatment success or no treatment until the next evaluation if they had, with a maximum continuous exposure of 24 weeks. Patients who did not achieve treatment success after 24 weeks continuous treatment were discontinued.

RESULTS: Only 26 (4.7%) patients discontinued at Week 12 due to lack of efficacy. Only one fifth (20.9%) of patients stopped treatment at 24 weeks. The incidence of skin AEs peaked around Day 60, remaining stable from Day 90 until study end. Treatment-related AEs reported by ³2% of patients within any designated treatment period included application site dermatitis, pruritus, and pain. Treatment-emergent serious AEs were noted in 3.3% of patients; none considered treatment-related. No deaths were reported, and no clinically noticeable trends identified with regard to other local skin AEs (e.g., skin atrophy, folliculitis, telangiectasia, and striae). AEs were not correlated with the timing and/or duration of treatment applications, frequency, and duration of use. Marked improvements in baseline severity of itching, dryness, and burning/stinging occurred within 2 weeks that were sustained over the course of the study.

CONCLUSIONS: HP/TAZ lotion has a favorable long-term safety profile in subjects with moderate-to-severe psoriasis when followed for 1 year. Although AEs reported were consistent with a product containing TCS and retinoid, they occurred low frequencies.

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DISCLOSURES: Mark Lebwohl: is an employee of Mount Sinai which receives research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen / Johnson & Johnson, Leo Pharmaceutucals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, UCB, Valeant, and ViDac. Dr. Lebwohl is also a consultant for Allergan, Aqua, Arcutis, Boehringer-Ingelheim, LEO Pharma, Menlo, and Promius. Jeffrey Sugarman: is an adviser or speaker for Valeant, Pfizer, and Promius. Linda Stein Gold: is and advisor, consultant, and speaker for Valeant Pharmaceuticals. Pariser: is an advisor, consultant, and speaker for Valeant Pharmaceuticals. Tina Lin, Radhakrishnan Pillai, Gina Martin, Susan Harris, Robert Israel are all employees of Bausch Health.

PA-31: Microbiome Dysbiosis as a factor in Rosacea Pathogenesis: A Pilot Study of Twins

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BACKGROUND: Rosacea is a relatively common, chronic inflammatory disorder of the central face, characterized by transient or persistent erythema and telangiectasias, papules and/or pustules, phymatous changes and ocular manifestations that has been theorized to correlate with other inflammatory conditions. The current pathophysiologic model incorporates both environmental and genetic components including alcohol consumption, history of smoking, hyper-reactive neurovasculature, overactivity of the innate immune system, and inflammatory reactions to the skin microbiome and dysbiosis. Previous studies have demonstrated a correlation between rosacea and dysbiosis of both the facial cutaneous and enteral microbiome.

OBJECTIVE: We sought to determine correlations between changes in collected facial cutaneous and enteral microbiome samples and the severity and concordance of rosacea between twin siblings with and without rosacea (intra-twin variability, IaV) and between different sets of twin siblings with and without rosacea (inter-twin variability, IV). In addition, we used questionnaires and survey data to identify potential environmental factors that alter the facial cutaneous or enteral microbiome.

METHODS: Identical and fraternal twins with and without rosacea, as determined by a board-certified dermatologist, were surveyed during the Twins Day festival in Twinsburg, OH in August 2017 about their history of rosacea as well as environmental factors with potential to alter their facial cutaneous and enteral microbiome. Demographic analysis was performed using R. P-values were calculated based on t.test for pairwise comparisons or X2 test for multiple categories comparisons. To ensure robustness, linear regression was applied resulting in strong statistical concordance between methods. Facial skin and gut microbiome data were collected and analyzed for 16S sequences clustered into Operational Taxonomic Units (OTUs) at a similarity cutoff value of 97% using the UPARSE algorithm. OTUs were mapped to an optimized version of the SILVA and UNITE Databases. Downstream analysis was performed using R. Custom script was used to identify trends in taxa abundance, alpha-diversity, and beta-diversity. Significance of categorical variables was determined using the non-parametric Mann-Whitney U test and/or the Kruskal-Wallis test. Ordination method was based on principal coordinates analysis (PCoA) followed by Monte Carlo permutation test for p-value estimation. Differential abundance was calculated using DESeq2. P-values were adjusted for multiple comparisons with Benjamini-Hochberg FDR correction.

RESULTS: In total, our pilot study included 128 individuals (Rosacea, N = 84; Control, N = 44). We found individuals with rosacea show decreased richness and evenness (Raw Counts: p = 0.019; Shannon: p = 0.049) in facial cutaneous microbiome compared to control. Furthermore, there was a 3 to 4-fold decrease in abundance of facial cutaneous bacterial genera Streptococcus (FDR = 0.015; FDR = 0.004), Cornyebacterium (FDR = 0.003), Actinomyces (FDR = 0.015), Lactococcus (FDR = 0.016), Veillonella (FDR < 0.001) and Chloroplast (FDR = 0.015) in rosacea compared to control. In the gut microbiome, there was significant reduction in abundance of Ruminococcaceae (8-fold reduction; FDR = 0.002) and Blautia (2-fold reduction; FDR < 0.001) and a 6-fold increase in Prevotellaceae (FDR = 0.024) in rosacea compared to control. We found no significant difference in bacterial load in the facial cutaneous microbiome (p = 0.36) or enteral microbiome (p = 0.29)

between rosacea (average face count, 30,880; average gut count 14198) or control (average face count, 29,533; average gut count, 13,566). Individuals with rosacea are more likely to currently own pets ($p = 0.029$), have a lower Fitzpatrick score ($p < 0.001$) and consume more alcohol ($p = 0.006$) than their control counterparts.

LIMITATIONS: Our pilot study was conducted with a limited sample size which may have led to insufficient power for analysis. Furthermore, almost 50% (n= 43) of participants with active rosacea were graded as "mild" and might not present with sufficiently robust inflammation or dysbiosis for detection.

CONCLUSION: Studies have shown that dysbiosis and decreased microbiome diversity have been associated with numerous other dermatoses. In this preliminary study we were able to show that individuals with rosacea are more likely to have decreased facial microbiome diversity and are more likely to be current pet owners. Our preliminary results were able to determine few differences on the genus level in facial and gut microbiomes between rosacea and control. While the current results are not entirely conclusive, reduction in abundance of specific facial cutaneous microbial genera could be a cause of the observed differences in diversity between rosacea and control, especially since we found no significant difference in bacterial load between rosacea and control. We speculate that losses in the six-observed facial cutaneous genera may be supplanted by increased abundance in other measured genera, thereby decreasing evenness and richness. We plan to return to the next Annual Twin's Day Festival in August 2018 to recruit additional participants, particularly those with moderate and severe rosacea to further study correlation between alterations in the microbiome and rosacea severity.

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PA-32: New-Onset of Erythematous Indurated Plaques in a Patient with History of Breast Cancer and Radiotherapy

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BACKGROUND: Radiation-induced morphea (RIM) is a rare, under-recognized complication of radiotherapy characterized by inflammation and sclerosis of affected tissues. Affects 1/500 (0.2%) of patients with breast cancer s/p radiotherapy. The specific etiology remains unknown, but it has been reported radiation injures fibroblast and endothelial cells triggering the release of cytokines and growth factor, including TGF-B, leading to an overproduction of collagen and inhibition of its degradation causing fibrosis of the exposed normal tissue. Few published studies exist regarding the occurrence of RIM at a distant body site from previous radiation treatment.

CASE REPORT: A 68-year-old female with previous medical history of HTN and right breast cancer was evaluated due to an 8-month history of an erythematous, indurated plaques over right breast. Also, patient reported a 1-month history of similar lesions on abdomen and bilateral flanks. Breast cancer was treated 7 years ago with lumpectomy, axillary lymph node dissection, and radiotherapy and received tamoxifen for a 5-year span. Examination showed a tender, erythematous, indurated plaque extending from right breast to abdomen without epidermal changes. Rheumatologic work-up for systemic disease was unremarkable.

Skin biopsy showed a superficial, mild, perivascular lymphocytic infiltrate associated with dermal fibrosis and thickened collagen bundles. Bilateral breast MRI was performed which showed no evidence of malignancy recurrence. After a clinico-pathological correlation the most likely diagnosis was RIM. Patient was started in UVA therapy with clinical improvement.

DISCUSSION: Although uncommon, the development of morphea presenting as erythematous indurated plaques at a distant site of radiation treated site may still occur. As such, this diagnosis should always be considered in patients with history of radiation and therefore, must be differentiated from other diseases like malignancy recurrence, post-irradiation fibrosis, chronic radiation dermatitis, radiation recall dermatitis, and acute and subacute radiation dermatitis, among others. Early recognition and diagnosis is important in order to avoid unnecessary test and begin prompt treatment. Further research of pathogenesis and therapy may provide additional insight into the risk factors and prognosis of patient with this disease.

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DISCLOSURES: Dr. Falto has nothing to disclose. Dr. Carrasquillo has nothing to disclose. Dr. Martin has nothing to disclose. Dr. Arias has nothing to disclose.

PA-33: 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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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.

MATERIALS/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 noninflammatory 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 noninflammatory 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 noninflammatory 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 four weeks and appeared to be transient.

CONCLUSIONS: Tretinoin 0.05% lotion was significantly more effective than its vehicle in achieving treatment success and reducing inflammatory and noninflammatory lesions in female acne. Noninflammatory 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.

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DISCLOSURES: Leon Kircik: has been a consultant and investigator for Valeant Pharmaceuticals. Hilary Baldwin: is an advisor and consultant for Valeant Pharmaceuticals. Eric Guenin, Varsha Bhatt are employees of Bausch Health.

PA-34: Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in a Preadolescent Population

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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.

MATERIALS/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 noninflammatory 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 noninflammatory 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.

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

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DISCLOSURES: Lawrence Eichenfield: is an advisor, consultant, and speaker for Valeant Pharmaceuticals. Jeffrey Sugarman: is an adviser or speaker for Valeant, Pfizer, and Promius. Eric Guenin, Varsha Bhatt are employees of Bausch Health.

PA-35: Outcomes of Pregnancies from Tildrakizumab Phase 1–3 Clinical Development Program

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BACKGROUND: Tildrakizumab, a high-affinity, humanized, immunoglobulin G1κ, anti–interleukin-23p19 monoclonal antibody, has demonstrated efficacy in the treatment of moderate to severe

chronic plaque psoriasis in 3 large clinical trials: P05495 (phase 2b; NCT01225731)1, reSURFACE 1 (phase 3; NCT01722331)2, and reSURFACE 2 (phase 3; NCT01729754)2. The clinical data concerning human exposure to tildrakizumab during pregnancy are currently very limited.

OBJECTIVE: To evaluate pregnancy outcomes in women exposed to tildrakizumab, specifically cases of spontaneous abortion and congenital anomalies reported in the tildrakizumab clinical development program.

MATERIALS/METHODS: Inclusion criteria included mandatory contraception for participants of both genders for cases in which at least 1 partner was a woman of childbearing age. Female patients who were pregnant, intended to become pregnant (within 6 months of completing the trial), or were lactating were excluded from enrollment into the clinical trials. However, the patients who became pregnant during the clinical trials (protocol violators) were categorized, and pregnancy outcome data were evaluated. Data were collected from patients who participated in the following tildrakizumab clinical trials: P05661, P05776, and P06306 (in healthy volunteers); P05839 (in patients with Crohn's disease); and P05382, P009, P05495, reSURFACE 1, and reSURFACE 2 (in patients with psoriasis).

RESULTS: Among 528 female patients receiving tildrakizumab through phases 1–3, a total of 13 pregnancies were reported. These included patients for whom contraception failed (n=5) and patients who did not use contraception (n=8). A total of 2 pregnancies occurred in the phase 1 trials (1 in each of the 2 trials P05661 and P05839), and 11 pregnancies occurred in the phase 2b/3 trials, ie, 2 pregnancies in P05495, 5 pregnancies in reSURFACE 1, and 4 pregnancies in reSURFACE 2. The duration of exposure to tildrakizumab was variable in these patients, with the longest duration being for a patient who had received 11 doses of tildrakizumab 100 mg, with the last dose received on Day 784. Medication was immediately stopped after confirmation of pregnancy in these patients. Outcomes were reported for all 13 pregnancies; these included 6 cases of fetal loss—2 spontaneous abortions (15.4%) and 4 elective abortions (30.8%)—and 7 full-term live births with no identifiable congenital anomalies (53.8%).

CONCLUSIONS: In summary, although contraception in female patients of childbearing age was mandatory prior to initiation of tildrakizumab therapy, some pregnancies occurred during the tildrakizumab clinical development program as protocol violations. The rate of spontaneous abortion (15.4%) was similar to that seen in the general population (12%–15%).3 All of the pregnancies that continued to full term resulted in healthy babies with no congenital anomalies.

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DISCLOSURES: KH has been a member of the advisory committees for Celgene, Lilly, Pfizer, Sun Pharmaceuticals, AbbVie, and Valeant, and has served as a speaker for Lilly. MB has served as a consultant for Sun Pharmaceuticals, and as an advisor/speaker for AbbVie, Celgene, EPI Health, Galderma, ISDIN, Promius Pharma, Lilly USA, Novartis, Ortho Dermatologics, Taro, and Pfizer. DD has been a member of advisory committees for Novartis, Celgene, and Ortho Dermatologics. SJR and AMM are employees of Sun Pharmaceutical Industries, Inc. TB has served as investigator for Janssen, Merck, Lilly, and Strata Life Sciences. The studies were funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; analyses funded by Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA.

ACKNOWLEDGMENTS: Analyses were presented at the DERM 2018 NP/PA Conference, July 19–22, 2018, Las Vegas, NV, USA.

PA-36: Patient-Reported Outcomes among Patients with Hidradenitis Suppurativa (HS) Experiencing Different Levels of Clinical Response: Integrated Analysis from 2 Clinical Studies

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disease with painful lesions in the apocrine gland-bearing regions of the body, which lead to significant decreases in quality of life. Two phase 3 trials showed that treatment with adalimumab (ADA) results in significantly higher clinical response rates, assessed by reduction in total abscess and inflammatory nodule count (AN), as well as patient reported outcomes (PROs). However, it is unclear whether patients with different levels of clinical improvement also experience corresponding improvements in PROs.

OBJECTIVE: To assess PROs among patients with varying levels of clinical response using integrated data from 2 randomized, placebo-controlled, phase 3 trials: PIONEER I and II.

MATERIALS/METHODS: This post hoc analysis included all patients treated with either ADA (40 mg weekly) or placebo for the first 12 weeks of both studies (period A, N = 633). Patients were stratified based on percent reduction in total AN count from baseline (BL) to week 12 (AN 25 to <50, AN 50 to <75, AN 75 to <100, or AN 100). PROs assessed included HS-related Patient's Global Assessment of Skin Pain at worst (numeric rating scale [NRS], among patients with BL value ≥ 3, range 0 [no skin pain] to 10 [worst skin pain]), and Dermatology Life Quality Index (DLQI).

RESULTS: Mean percent changes from BL in NRS scores for both AN 25 to <50 and AN 50 to <75 were –14.1 at week 12. Changes in NRS scores were greater for AN 75 to <100 and AN 100 (–35.8 and –50.8, respectively). Mean changes from BL in DLQI for AN 25 to <50, AN 50 to <75, AN 75 to <100, and AN 100 were –3.1, –4.7, –6.1, and –7.5, respectively. All groups demonstrated significant mean changes from BL in both NRS and DLQI scores ($P < .001$).

CONCLUSIONS: Overall, higher percent changes in AN counts (AN 75 to <100 and AN 100), were associated with greater reductions in HS-related skin pain and DLQI. Patients with a lower clinical response (AN 25 to <50) experienced similar improvements in skin pain as did those with a higher response (AN 50 to <75). Additionally, all patients who demonstrated clinical improvements, regardless of magnitude, demonstrated significant improvements in DLQI, and groups with higher responses achieved the minimal clinically important difference. Together, these results suggest that all ranges of improvements in AN counts result in improvements in PROs, as observed with HS-related skin pain and DLQI scores.

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DISCLOSURES: Thrasivoulos Tzellos has been reimbursed by Janssen, MSD, and Novartis for travel expenses and hotel accommodation to attend dermatological congresses. He also par-

ticipates as an advisor on AbbVie, Inc's., hidradenitis suppurativa advisory board. J. Sobell has received honoraria and research grants as a consultant, speaker, and/or investigator from AbbVie, Amgen, Eli Lilly, Celgene, Janssen Pharmaceuticals, Inc., Merck & Co., and Novartis International AG. Jen-fue Maa, Rakesh Singh, and Gerit Mulder are full-time employees of AbbVie, and may own stock and/or stock options in AbbVie. AbbVie funded this study and participated in the study design, study research, data collection, analysis and interpretation of data, and writing, reviewing, and approving this abstract for presentation. All authors had access to the data; participated in the development, review, and approval of the abstract; and agreed to submit this abstract to the American Academy of Dermatology for consideration as an oral presentation or poster. AbbVie and the authors thank the patients who participated in the trials and all study investigators for their contributions. Medical writing assistance, funded by AbbVie, was provided by Kavitha N Rao, PhD, and Kristy A Grabowski, PhD, of JB Ashtin.

PA-37: Pharmacokinetic and Exposure-Response Analyses for Extrapolation of Efficacy of Adalimumab in Adolescent Patients with Hidradenitis Suppurativa

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OBJECTIVE: Pharmacokinetic (PK) and exposure-response analyses were performed to allow extrapolation of adalimumab (ADA) efficacy and support dosing recommendation in adolescent HS patients (pts) using PK and efficacy data from adult HS pts and PK data from other pediatric populations.
MATERIALS/METHODS: A population PK model was developed based on ADA PK data (524 pts aged 2-17 years) in other pediatric indications (pediatric psoriasis, Crohn's disease, polyarticular juvenile idiopathic arthritis, and enthesitis-related arthritis). Factors affecting ADA PK were identified, then PK simulations were performed to predict ADA concentrations in adolescent HS pts to determine a dosing regimen that achieve concentrations similar to those observed in adult HS pts. Following extrapolation of ADA PK from other pediatric populations to adolescent HS pts, ADA efficacy was extrapolated from adult to adolescent HS pts. ADA serum concentrations and HS Clinical Response (HiSCR) rates from adult HS Phase 3 studies were used to develop a PK-pharmacodynamic (PD) model that characterized exposure-response relationship for ADA in adult HS pts. Assuming similar exposure-response relationship between adult and adolescent HS pts, PK-PD model was used to predict clinical outcomes in adolescent HS pts.
RESULTS: Results of pediatric PK model demonstrated that significant factors affecting ADA PK were body size, albumin, methotrexate co-administration, and development of immunogenicity. PK parameters were not different between disease indications, suggesting ADA PK in adolescent HS pts can be extrapolated from other pediatric populations. Simulation results showed predicted ADA steady state concentrations (mean±SD) in adolescent HS pts (8.4 ± 5.2 µg/mL) were similar to those observed in adult HS pts (8.8 ± 6.3 µg/mL) at a dosing regimen of 80 mg (Week 0), then 40 mg every other week (eow) (from Week 1). Results of simulations based on developed exposure-response model showed that predicted HiSCR rates in adolescents were 55% and 28% after 12 weeks of ADA treatment (80 mg, then 40 mg eow) and placebo, respectively. Rates were similar to overall response rates observed for adults in Phase 3 HS studies (51% and 27% after 40 mg every week and placebo dosing, respectively).
CONCLUSIONS: Population PK and exposure-response modeling and simulation analyses enabled extrapolation of ADA efficacy from adults to adolescent HS pts in the absence of clinical trial data in the adolescent HS population. Based on the predicted ADA concentration and efficacy in adolescent HS pts, a dosing regimen of 80 mg at Week 0 and 40 mg eow is expected to provide similar ADA exposure and efficacy in adolescent HS pts to those observed in adult HS pts.
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DISCLOSURES: N Vijay, A Nader, B Kleunder, C Wegzyn, and N Mostafa each receive a salary as employees of AbbVie, and may also receive AbbVie stock 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.

PA-38: Phase 1 Study of Cemiplimab, a Human Monoclonal Anti-PD-1, in Patients with Unresectable Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma (CSCC): Final Efficacy and Safety Data

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BACKGROUND: Initial analysis of expansion cohorts (ECs) patients in a phase 1 study showed that cemiplimab (REGN2810) demonstrated a positive risk/benefit profile and produced antitumor activity in patients (pts) with advanced CSCC. We now report mature final data from the CSCC ECs of the phase 1 study (NCT02383212).
MATERIALS/METHODS: Pts with distantly metastatic and locally/regionally advanced CSCC were enrolled in EC 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 according to RECIST 1.1 to determine overall response rate (ORR; complete response [CR] + partial response [PR]). The data cut-off date was Oct 02, 2017. Tumor response was assessed by an independent central review committee.
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 1 in 16 pts and 0 in 10 pts). Median duration of cemiplimab exposure was 36.0 weeks. The most common treatment-related adverse event (TRAE) of any grade was fatigue (26.9%). The following ≥Grade 3 TRAEs occurred once: asthenia, maculopapular rash, increased alanine aminotransferase, increased aspartate aminotransferase, adrenal insufficiency, and myalgia. ORR was 50.0% (95% CI: 29.9–70.1); 0 CR and 13 PRs. Disease control rate (DCR; ORR + stable disease [SD] + non-CR + non-progressive disease [PD]) was 76.9% (95% CI: 56.4–91.0); 6 SD and 1 non-CR/non-PD. Durable DCR (SD/non-CR/non-PD or response for ≥105 days) was 65.4% (95% CI: 44.3–82.8). 3 pts were not evaluable for response. The median duration of response has not been reached; however, for pts with PR, the duration of response exceeded 6 months in 7 pts and 12 months in 2 pts. Median time to response was 2.3 months (range, 1.7–7.3). Median duration of follow-up was 11.0 months (range: 1.1–17.0).
CONCLUSIONS: In this study, cemiplimab demonstrated a positive risk/benefit profile and produced substantial antitumor activity as well as durable responses in pts with advanced CSCC.
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DISCLOSURES: Taofeek K. Owonikoko: has received fees for a 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, PsiOxus, Nanobiotix, Janssen, Abbvie, PharmaMar, PUMA, Sanofi, Lilly, Pfizer, Merck, Nektar, Amcure, Amgen, AstraZeneca, Principia, Bayer, CytomX, H3, Incyte, Kura, LOXO, Macrogenics, Menarini, Merck, Serono, Merus, Millenium, Rigontec, Tahio, 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., Pharmacyclics, 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: has received advisory board fees from Regeneron Pharmaceuticals Inc. Daruka Mahadevan: has received speakers' bureau and travel, accommodation expenses from Abbvie. Jiaxin Niu: has received consulting or advisory role fees from Genentech, Biodesix, Paradigm, Ignyta, AstraZeneca and Teueda. Kosalai 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, 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-39: 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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BACKGROUND: 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 favourable tolerability in a phase 1 study of patients with advanced malignancies (NCT02383212).
TRIAL DESIGN: We are conducting a phase 2, non-randomised, 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. 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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DISCLOSURES: Karl D. Lewis: research funding and consulting fees from Regeneron Pharmaceuticals, Inc. Matthew Fury: a shareholder and an employee of, and holds patents, royalties, other intellectual property from Regeneron Pharmaceuticals, Inc. Elizabeth Stankevich: is an employee and shareholder of and has received accommodation and travel expenses from Regeneron Pharmaceuticals, Inc. Melissa Mathias: a shareholder and an employee of Regeneron Pharmaceuticals, Inc. Kosalai K. Mohan: a shareholder and an employee of Regeneron Pharmaceuticals, Inc. Siyu Li: employee and shareholder of Regeneron Pharmaceuticals, Inc. Katharine Nunnink: a shareholder and an employee of Regeneron Pharmaceuticals, Inc. Christina Perry: a shareholder and an employee of Regeneron Pharmaceuticals, Inc. Ameet Narwal: a shareholder and an employee of Regeneron Pharmaceuticals, Inc.

PA-40: Prevalence of Psoriatic Arthritis and Challenging-to-Treat Areas Among Patients With Psoriasis Who Initiated Biologic Therapy in the Corrona Psoriasis Registry

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BACKGROUND: Psoriasis localized in certain areas of the body such as scalp, nail, and palmoplantar is difficult to treat, and often requires systemic treatments. Up to 30% of patients with psoriasis may develop psoriatic arthritis (PsA), as well. The presence of PsA or psoriasis in challenging-to-treat (CTT) areas can make treatment decisions difficult for patients with psoriasis. Currently, real-world data for these patients are limited.

OBJECTIVE: To determine the prevalence of PsA and CTT localizations of psoriasis (scalp, nail, and palmoplantar) among patients with psoriasis who initiated biologic therapy in the US-based Corrona® Psoriasis Registry.

MATERIALS/METHODS: All patients aged ≥ 18 years diagnosed with psoriasis by a dermatologist who were enrolled in the Corrona Psoriasis Registry between April 2015 and May 2018 and initiated a biologic therapy at the time of enrollment were included. Patient demographics, clinical characteristics, treatment history, disease activity measures, and patient-reported outcome measures were assessed at registry enrollment. The proportions of patients with dermatologist-reported PsA and/or ≥ 1 CTT area were summarized using frequency counts and percentages.

RESULTS: A total of 2042 patients were included in the analysis. The overall mean (SD) age was 49.6 (14.7) years; 52% of patients were male, 80% were white, and 51% were obese (body mass index ≥ 30 kg/m2). Patients had a mean (SD) psoriasis disease duration of 19.9 (13.5) years, and the majority (89.2%) had moderate to severe disease, as assessed by a percentage of affected body surface area ≥ 3%. Of the 2042 included patients, 784 (38.4%) had PsA, 778 (38.1%) had scalp psoriasis, 326 (16.0%) had nail psoriasis, and 223 (10.9%) had palmoplantar psoriasis; 535 patients (26.2%) had a combination of ≥ 2 of these CTT areas and PsA. When examining the prevalence of mutually exclusive combinations of PsA and CTT areas, the most prevalent combinations were PsA alone (20.9%), scalp psoriasis alone (14.5%), PsA + scalp psoriasis (7.1%), scalp + nail psoriasis (5.2%), and PsA + nail and scalp psoriasis (4.9%); all other combinations were present in < 3% of the cohort.

CONCLUSIONS: Among 2042 patients with psoriasis who initiated biologic therapy in the Corrona Psoriasis Registry, nearly two-thirds had PsA and/or ≥ 1 CTT area. These results indicate a need to further characterize patients with psoriasis who have PsA and CTT areas and evaluate the impact of these factors to better understand their treatment needs.

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DISCLOSURES: K. Callis Duffin is an investigator and consultant for AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sienna, Steifel, and UCB. R. R. McLean, R. W. Harrison, and M. Crabtree are employees of Corrona, LLC. K. Gordon is an investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, and Janssen, and a consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Janssen, Novartis, and Pfizer. A. Guana and R. Germino are employees of Novartis Pharmaceuticals Corporation. M. Lebwohl is an employee of Icahn School of Medicine at Mount Sinai, which receives research funds from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen/Johnson & Johnson, Kadmon, Medimmune/AstraZeneca, Novartis, Pfizer, Valeant, and Vidac; and is also a consultant for Allergan plc, Aqua, Corrona, Leo Pharma, and Promius. Corrona, LLC, has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Roche, UCB, and Valeant. The design and conduct of the study was a collaborative effort between Corrona and Novartis, and financial support for the study was provided by Novartis. Novartis participated in the interpretation of data and review and approval of the abstract.

ACKNOWLEDGMENTS: Patients in the Corrona Psoriasis Registry are routinely seen and treated by dermatologists voluntarily participating in the registry and therefore may not be representative of all patients with psoriasis in the United States. Only patients with psoriasis who were being treated with biologic therapy were included in this analysis.

PA-41: 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 the 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).

MATERIALS/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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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-42: Primary Results from a Phase 2b, Randomized, Placebo-Controlled Trial of Upadacitinib for Patients with Atopic Dermatitis

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BACKGROUND: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritic skin lesions. The selective JAK-1 inhibitor, upadacitinib, is being investigated for treatment of patients with AD and other inflammatory indications.
MATERIALS/METHODS: In the first 16-week, double-blind portion of this 88-week, dose-ranging trial, adults with moderate-to-severe AD (EASI ≥16, BSA ≥10%, IGA ≥3) inadequately controlled by topical treatment, or for whom topical treatments were not medically advisable, were randomized to once-daily upadacitinib monotherapy 7.5, 15, or 30 mg, or placebo. Missing data were handled by last-observation-carried-forward (continuous variables) and non-responder-imputation (categorical variables).
RESULTS: Of the 167 randomized patients; 166 received study drug (42 in each upadacitinib dose-group; 40 in placebo). The primary efficacy endpoint, mean percentage improvement in EASI score from baseline to week 16, for upadacitinib 7.5/15/30mg groups was 39.4%/61.7%/74.4% vs 23.0% placebo ($p<0.05/<0.001/<0.001$). EASI 90 was achieved at week 16 by 14.3%/26.2%/50.0% upadacitinib patients vs 2.4% placebo ($p<0.05/p<0.01/p<0.001$). Mean percent improvement in pruritus from baseline to week 16 (measured by Numerical Rating Scale) was 39.6%/48.0%/68.9% upadacitinib vs 9.7% placebo ($p<0.01/<0.001/<0.001$). The most common adverse events (AEs), upadacitinib groups vs placebo, were upper respiratory tract infection (16.7%/11.9%/11.9% vs 10.0%) and AD exacerbation (16.7%/7.1%/11.9% vs 7.5%). 4.8%/2.4%/0% of upadacitinib patients (7.5/15/30mg groups) had serious AEs vs 2.5% placebo.
CONCLUSIONS: A clear dose-response was observed for upadacitinib efficacy in AD; the highest efficacy was achieved with 30 mg QD. The positive benefit/risk profile of upadacitinib supports proceeding with phase 3 trials in AD.

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DISCLOSURES: E Guttman, Honoraria; consultant: Regeneron, Sanofi, Stiefel/GSK, Pfizer,Galderma, Celgene, Leo Pharma,Dermira, Anacor,AnaptysBio,Glenmark, Novartis, Abbvie, Sun Pharma, Mitsubishi Tanabe, Vitae, Allergan, Almirall, Puricore, Asana Biosciences, Gilead, Concert, Immune, Kyowa Kirin, Ziarco, DS Biopharma, DBV Technologies. Research grants; investigator: Regeneron, Pfizer, Abbvie, Celgene, Medimmune, Leo Pharma, Glenmark, Vitae, Innovaderm, Immune, Novartis, Galderma, Dermira, Lilly, Asana. D Thaci: Honoraria; ad board, speaker, consultant: AbbVie, Almiral, Amgen, Bioskin, Boehringer-Ingelheim, Celgene, Galapagos, GSK, Dignity, Dermira, Janssen, Leo, Maruho, Medac, Morphosys, Lilly, Novartis, Pfizer, Regeneron/Sanofi, Samsung, Sandoz-Hexal, Sun-Pharma, UCB; Research grants; investigator: AbbVie, Celgene and Novartis. C Hong: Honoraria; ad board, speaker, consultant: Abbvie, Amgen, Celgene, Eli Lilly, Galderma, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron/Sanofi, Sun Pharma, Valeant; Research grants; investigator: Abbvie, Akros, Amgen, Cutanea, Celgene, DS Biopharma, Eli Lilly, Galderma, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Pfizer, Reneron/Sanofi, Roivant Sciences. J Silverberg: Honoraria; ad board, speaker, consultant: Abbvie, Eli Lilly, Galderma, GlaxoSmithKline, Kiniksa, Leo, Menlo, Pfizer, Realm-1, Roivant, Regeneron-Sanofi; Research grants; investigator: GlaxoSmithKline. M-E Mohamed, J Anderson, Y Gu, H Teixeira, A Othman, A Pangan: Salary, stocks, stock options; employee: AbbVie. 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.
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PA-43: Retreatment with Brodalumab Results in High Response Rates in Patients with Psoriasis after Treatment Interruption

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BACKGROUND: Brodalumab is a fully human anti–interleukin-17 receptor A (IL-17RA) monoclonal antibody that binds to IL-17RA, antagonizing the action of downstream inflammatory cytokines involved in psoriasis pathogenesis. In patients with moderate-to-

severe psoriasis, continuous treatment with brodalumab has been shown to be highly efficacious.
OBJECTIVE: To present efficacy data following brodalumab withdrawal and retreatment.
MATERIALS/METHODS: In this phase 3, double-blind, placebo-controlled study (NCT01708590; AMAGINE-1), patients with moderate-to-severe psoriasis were randomized to brodalumab (140 or 210 mg) or placebo every 2 weeks (Q2W) during a 12-week induction phase.1 At week 12, patients receiving brodalumab who achieved a static physician's global assessment (sPGA) score of 0 or 1 were rerandomized to their induction dose of brodalumab or placebo. Beginning at week 16, all re-randomized patients who experienced return of disease (sPGA ≥3) qualified for retreatment and received an induction dose of brodalumab.
RESULTS: A total of 79 patients randomized to brodalumab 210 mg Q2W in the induction phase and re-randomized to placebo in the withdrawal phase experienced return of disease. Of the patients who exhibited psoriasis area and severity index 75% improvement from baseline (PASI 75) prior to brodalumab 210 mg withdrawal (n=38), 92.1% achieved PASI 75 (95% confidence interval [95% CI], 78.6%-98.3%), 86.8% achieved PASI 90 (95% CI, 71.9%-95.6%), and 65.8% achieved PASI 100 (95% CI, 48.6%-80.4%) 16 weeks after reinitiation of brodalumab 210 mg. For patients who were initially PASI 90 responders (n=34) at 12 weeks of treatment, 91.2% achieved PASI 90 (95% CI, 76.3%-98.1%) and 73.5% achieved PASI 100 (95% CI, 55.6%-87.1%) 16 weeks after reinitiation of brodalumab 210 mg. For those who reached PASI 100 with initial treatment (n=21), 90.5% achieved PASI 100 (95% CI, 69.6%-98.8%) 16 weeks after reinitiation of brodalumab 210 mg.
CONCLUSIONS: For patients with psoriasis who experienced a return of disease following brodalumab withdrawal, most returned to their previous levels of response 16 weeks following reinitiation of brodalumab. These results are relevant to real-life practice because it is relatively common for patients to stop and restart their medications for a variety of factors.
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DISCLOSURES: April Armstrong has served as a consultant for AbbVie, Amgen, Janssen, Merck & Co, Eli Lilly & Co, Novartis, and Pfizer and has served as an investigator for AbbVie, Janssen, and Eli Lilly & Co and as a member of the speaker's bureau for AbbVie. Andrew Blauvelt has served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly & Co, Galderma, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Meiji, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac and as a paid speaker for Janssen, Regeneron, and Sanofi Genzyme. Jashin J. Wu is an investigator for AbbVie, Amgen, Eli Lilly & Co, Janssen, Novartis, and Regeneron. Brian R. Keegan has served as an investigator, advisory board member, and speaker for Bausch Health. Abbey Jacobson is an employee of Ortho Dermatologics and holds stocks and/or stock options in Bausch Health. Radhakrishnan Pillai is an employee of Dow Pharmaceutical Sciences and may hold stock and/or stock options in the company. Robert J. Israel is an employee of Bausch Health and holds stock and/or stock options in the company.

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PA-44: Risankizumab Efficacy/Safety in Moderate-to-Severe Plaque Psoriasis: 16-Week Results from IMMhance

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BACKGROUND: Risankizumab is a potent humanized IgG1 monoclonal antibody that inhibits IL-23 by specifically binding its p19 subunit. Here, we report efficacy and safety results of risankizumab from initial 16-week (wk) placebo (PBO)-controlled period of IMMhance trial in patients (pts) with moderate-to-severe chronic plaque psoriasis (PsO).
MATERIALS/METHODS: IMMhance (NCT02672852) is a phase 3 multicenter, randomized, double-blind, PBO-controlled trial, evaluating the efficacy and safety of risankizumab versus PBO in pts with moderate-to-severe chronic plaque PsO. The initial 16-wk PBO-controlled period (507 pts, stratified by weight and prior TNFi-exposure, randomized 4:1 to receive either risankizumab [150 mg at wks 0 and 4] or PBO) was followed by randomized withdrawal and subsequent re-treatment with risankizumab. Co-primary endpoints were PASI 90 and sPGA 0/1 responses at wk 16; missing data were imputed as non-responders.
RESULTS: At baseline, the mean age and weight were 49.2 years and 92.0 kg, respectively; 70.2% of pts were male. A history of diagnosed or suspected psoriatic arthritis was reported in 34.7% of pts and prior TNFi therapy was reported in 36.5% of pts. Mean

baseline PASI and BSA were 20.2 and 26.1%, respectively. At wk 16, all primary and ranked secondary endpoints were met (P<0.001). At Wk 16, risankizumab -treated pts achieved significantly higher PASI 90 (73.2%) and sPGA 0/1 (83.5%) response rates versus PBO-treated pts (2.0%; 7.0%). Treatment-emergent adverse events (TEAEs) and serious AEs were reported in 45.5% and 2.0% of risankizumab-treated pts, respectively. Through 16 wks, there were no deaths, major adverse cardiovascular events, or cases of tuberculosis in risankizumab-treated pts.

CONCLUSIONS: Risankizumab was superior to PBO in the treatment of adult pts with moderate-to-severe plaque PsO. The safety profile was consistent with previously reported risankizumab trials with no new or unexpected safety findings.

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DISCLOSURES: A Blauvelt has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, 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, Valeant, and Vidac. KA Papp has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Amgen, Astellas, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB, and Valeant. M Gooderham has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin Pharma, Leo Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Takeda, UCB, and Valeant. RG Langley has served as principal investigator for and is on the scientific advisory board of or served as a speaker for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Leo, Merck, Novartis, and Pfizer. C Leonardi has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Actavis, Amgen, Celgene, Coherus, Dermira, Eli Lilly, Galderma, Janssen, Leo, Merck, Novartis, Pfizer, Sandoz, Stiefel, UCB, and Wyeth. JP Lacour has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galderma, Janssen, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, and Sanofi. S Philipp has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Almirall, Amgen, Biogen, BMS GmbH, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, GSK, Hexal, Janssen Cilag, Leo Pharma, Maruho, MSD, Merck, Mundipharma, Novartis, Pfizer, UCB Pharma and VBL Therapeutics. S Tyring has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie and Boehringer Ingelheim. M Bukhalo has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from Allergan, Boehringer Ingelheim, Celgene, Centocor, DUSA Pharmaceuticals, Eli Lilly, Galderma, Leo Pharma, MedImmune, Merck, and Novartis. JJ Wu is an investigator for AbbVie, Amgen, Eli Lilly, Janssen, Novartis, and Regeneron. J Bagel has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Sun, and Valeant. EH Frankel has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie. D Pariser has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from Abbott Laboratories, Amgen, Bickel Biotechnology, Biofrontera AG, Celgene, Dermira, DUSA, Leo Pharma, Eli Lilly, Leo Pharma, Novartis, Novo Nordisk A/S, Ortho Dermatologics, Peplin, Pfizer, Photocure ASA, Promius, Regeneron Pharmaceuticals, Inc, Stiefel, TheraVida, and Valeant. M Flack and J Scherer are full-time employees of Boehringer Ingelheim. Z Geng, Y Gu, A Camez, and EHZ Thompson are full-time employees of AbbVie and may own stock/options.

PA-45: 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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BACKGROUND: Topical corticosteroids (TCS) are the mainstay of psoriasis treatment. Clinical trials have studied twice-daily dosing and both safety concerns and labelling limit consecutive use to 2-4 weeks.

OBJECTIVE: Investigate safety and efficacy of once-daily halobetasol propionate (HP) 0.01% lotion in moderate-to-severe plaque psoriasis.

MATERIALS/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 with HP lotion, the most common being application site dermatitis (0.7%).
CONCLUSIONS: Halobetasol propionate 0.01% lotion provides significant efficacy over 8 weeks, with good tolerability and safety.
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DISCLOSURES: Jeffrey Sugarman: is an adviser or speaker for Valeant, Pfizer, and Promius. Jonathan Weiss: is an advisor and consultant for Valeant Pharmaceuticals. Emil Tanghetti: no relevant conflicts. Jennifer Soung: has received research, speaking and/or consulting support from a variety of companies including Janssen, Eli Lilly, Amgen, AbbVie, Merz, Pfizer Inc, Galderma, Valeant, National Psoriasis Foundation, Cassiopea, Celgene, Actavis, Actelion, and GSK. Tina Lin, Gina Martin, Radhakrishnan Pillai, Susan Harris are all employees of Bausch Health.

PA-46: Safety Profile of Adalimumab for Moderate-to-Severe Plaque Psoriasis: Systematic Literature Review and Meta-Analysis

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BACKGROUND: Adalimumab is a recombinant human immunoglobulin monoclonal antibody that binds to the proinflammatory cytokine tumour necrosis factor-alpha (TNF-α). Adalimumab neutralises the biological function of TNF-α by blocking its interaction with the p55 and p75 cell-surface TNF receptors. The indication for adalimumab is the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to or who are intolerant to other systemic therapy including ciclosporin, methotrexate or PUVA. The outcomes stated in the manufacturer's definition of the decision problem were measures of severity of psoriasis, remission rate, adverse effects of treatment and health-related quality of life.
OBJECTIVE: To conduct a systematic literature review and meta-analysis of the controlled randomized clinical trials available regarding the safety of adalimumab used for moderate-to-severe plaque psoriasis.
MATERIALS/METHODS: PubMed, EMBASE and Cochrane Library, were used to retrieve relevant studies. The search was supplemented by a review of abstracts from AAD, EADV and PIN meetings between 2015 -2017. Treatment-related (AEs) data were extracted and the Q heterogeneity statistic was tested.
RESULTS: Our search yielded 1743 published articles and conferences, after abstract and text review, 9 randomized clinical trials with a total of 2888 patient (male= 61.5%; mean age= 44.54 ± 12.21) were eligible for final analysis. There was evidence of significant heterogeneity between studies. In 9 studies, Adalimumab was compared to placebo or biologic therapy and the random effect pooled RR for severe AEs was 0.020 (95% CI 0.011-0.030.; p= 0.187). In treatment group, infection, nasopharyngitis, URTI, headache, injection site reaction, and cancer were 26.27%, 6.69%, 3.9%, 4.05%, 0%, and 0.35% patients, respectively.
CONCLUSIONS: This systematic review evaluates the most common AEs of adalimumab using for treatment of plaque psoriasis. According to the safety results, adalimumab provides an important therapeutic alternative for treatment of moderate to severe plaque psoriasis.
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DISCLOSURES: I certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on me (or any other authors) or on any organization with which I (or any other authors) am associated. The authors have nothing to disclose.
ACKNOWLEDGMENTS: As published literature will be used in the analyses, there is a possible publication bias for positive results. To overcome the risk of bias, grey literature (conferences and trial registries) will additionally be searched. Moreover, systematic variation exists in patient and study characteristics across trials comparing different interventions that may not be able to be adjusted for in the NMA model. The strengths of the analysis are that all available evidence will be put together in one document and that an NMA allows conclusive synthesis of accumulating scientific evidence. Both the strengths and the weaknesses will be evaluated before the final decision on which data are to be used for the analysis.

PA-47: Safety Profile of Biologic Treatment for Moderate-to-Severe Plaque Psoriasis: Systematic Literature Review and Meta-Analysis

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BACKGROUND: Psoriasis is a chronic, immune-mediated skin disorder affecting 2- 3% of the population worldwide with the highest disease prevalence occurring in North America and Europe. The most common form of psoriasis is plaque-type psoriasis, present in 80% to 90% of patients and characterized by the presence of thick, scaly plaques. Approximately 20% of patients with psoriasis have moderate to severe disease. The severity of psoriasis is defined by the extent of the body surface area (BSA) involvement (more than 5% and less than 10% moderate, and ≥10% severe) and by involvement of the hands, feet, facial, or genital regions. Patients' perception of the physical and mental burden that the disease imposes on their life may be greater than that of cancer, arthritis, hypertension, heart disease, diabetes, and depression. Patients with severe psoriasis have an increased risk for mortality, largely attributable to cardiovascular death. With our increased understanding of the immunopathogenesis of psoriasis, multiple biologic agents have been introduced during last decade that target specific molecules necessary for the development of psoriatic plaques.
OBJECTIVE: To conduct a systematic literature review and me-

ta-analysis of the controlled randomized clinical trials available regarding the safety of biologic treatment used for moderate-to-severe plaque psoriasis.

MATERIALS/METHODS: PubMed, EMBASE and Cochrane Library, were used to retrieve relevant studies. The search was supplemented by a review of abstracts from AAD, EADV and PIN meeting between 2015 -2017. Treatment related (AEs) data were extracted and the Q heterogeneity statistic was tested using a chi-square test.

RESULTS: Our search yielded 3531 published articles and conferences, after abstract and text review, 48 randomized clinical trials with a total of 23679 patients (male= 58.3%; mean age=44.81 ± 12.74) were eligible for final analysis. There was evidence of significant heterogeneity between studies. In 38 studies, biologic treatment was compared to placebo and the random effect pooled RR for severe AEs was 0.025 (95% CI 0.019-0.031.; p< 0.001). In treatment group, infection, nasopharyngitis, URTI, headache, injection site reaction, and cancer were 21.76%, 7.25%, 5.15%, 6.19%, 2.78%, and 0.23% patients, respectively. In 10 studies (5515 patients, male= 65.9%) biologic treatment was compared to biologic or conventional therapy. Severe AEs was reported in 0.04 % of cases. The most common AEs were infection, nasopharyngitis, headache, injection site reaction, URTI, and fatigue. Cancer was reported in 0.01 cases.

CONCLUSIONS: This systematic review evaluates the most commonly AEs of biological drugs using for treatment of plague psoriasis. According to the safety results, biological agents provide an important therapeutic alternative for treatment of moderate to severe plaque psoriasis.

LIMITATIONS/STRENGTHS: As published literature will be used in the analyses, there is a possible publication bias for positive results. To overcome the risk of bias, grey literature (conferences and trial registries) will additionally be searched. Moreover, systematic variation exists in patient and study characteristics across trials comparing different interventions that may not be able to be adjusted for in the NMA model. The strengths of the analysis are that all available evidence will be put together in one document and that an NMA allows conclusive synthesis of accumulating scientific evidence.Both the strengths and the weaknesses will be evaluated before the final decision on which data are to be used for the analysis

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PA-48: Secukinumab Shows High and Sustained Efficacy in Nail Psoriasis: 2.5-Year Results From the TRANSFIGURE Study

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BACKGROUND: Nail psoriasis is associated with decreased finger mobility, functional impairment, pain, and reduced quality of life (QoL), and is often difficult to treat. It correlates with more severe psoriatic disease and is an important predictor of psoriatic arthritis (PsA). Nails are affected in up to 50% of psoriasis patients, with a lifetime incidence as high as 90%.1 Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, has demonstrated significant efficacy in the treatment of moderate to severe psoriasis and PsA, demonstrating a rapid onset of action and sustained responses with a favorable safety profile.

OBJECTIVE: Here we report the long-term follow-up efficacy and safety results from the TRANSFIGURE study, the first robust (2.5-year) data reported in subjects with nail psoriasis treated with secukinumab.

MATERIALS/METHODS: TRANSFIGURE 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 moderate to severe nail psoriasis, involving 198 subjects.

RESULTS: As previously reported, at Week 16 the primary endpoint NAPSI (NAil Psoriasis Severity Index) and all secondary endpoints of this study were met, demonstrating superiority of secukinumab to placebo after 16 weeks' placebo-controlled treatment.2 An interim analysis at Week 80 demonstrated the continuation of improvement in nail psoriasis for all efficacy parameters. The effect was sustained through 2.5 years with a large mean NAPSI improvement from baseline of –73.3% and –63.6% with secukinumab 300 and 150 mg, respectively (as observed). Secukinumab demonstrated sustained reductions (improvements) in total mean NAPPA (Nail Assessment in Psoriasis and Psoriatic Arthritis) QoL scores from baseline to 2.5 years by –52.4% and –18.1%, and 70.2% and 71.0% of subjects achieved a weighted NAPPA-PBI (Patient Benefit Index) global score of ≥2 (at least moderate benefits) with secukinumab 300 and 150 mg, respectively (last observation carried forward). Subjects showed considerable improvements in EQ-5D (EuroQoL 5-Dimension Health Status Questionnaire) compared with baseline reporting decreased pain and discomfort. The safety profile was consistent with that observed in previous phase 3 trials of psoriasis and PsA.

CONCLUSIONS: TRANSFIGURE is the first large, randomized controlled trial to report long-term results in subjects with nail psoriasis. Secukinumab demonstrated strong sustainability of clinically meaningful efficacy, large QoL improvement, and a favorable safety profile up to 2.5 years in difficult-to-treat nail psoriasis.

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Merck Sharp & Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoport. P Arenberger: Grants from Novartis. S Jazayeri: Participated in clinical trials sponsored by Boehringer, Lilly, Novartis; speaker for Novartis. M Augustin: Grants and/or participated in clinical trials for AbbVie, Almirall, Amgen, Biogen Idec, Boehringer-Ingelheim, Celgene, Centocor, Eli Lilly, Janssen-Cilag, Leo, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), Pohl Boskamp, Sandoz, Xenoport; advisor and/or received speaker honoraria from AbbVvie, Almirall, Amgen, Biogen Idec, Boehringer-Ingelheim, Celgene, Centocor, Eli Lilly, Janssen-Cilag, Leo, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), Pohl Boskamp, Sandoz, Xenoport. P Regnault, R You, J Frueh: Employees of Novartis.

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PA-49: 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.1 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.
OBJECTIVE: 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.
MATERIALS/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.
RESULTS: As previously reported, after 16 weeks' placebo-controlled treatment, the primary endpoint palmoplantar Investigator's Global Assessment (ppIGA) 0/1 and all secondary endpoints of this study were met, demonstrating superiority of secukinumab to placebo at Week 16.2 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 was 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 feet 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.
CONCLUSIONS: 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 ppPsO population by providing a strong and sustained response through 2.5 years.
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PA-50: Subcutaneous Secukinumab Inhibits Radiographic Progression in Psoriatic Arthritis: Analysis by Prior Anti–TNF Therapy and Concomitant Methotrexate Use

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BACKGROUND: Psoriatic arthritis (PsA) is associated with joint inflammation, characterized by synovitis, presence of erosions,

joint space narrowing (JSN), and new bone formation leading to structural damage, increased disability, and reduced quality of life. Secukinumab (SEC) provided significant and rapid clinical efficacy, and inhibition of radiographic progression, in PsA patients in the FUTURE 5 study.1

OBJECTIVE: To assess the effect of subcutaneous (s.c.) secukinumab on radiographic progression by prior anti–TNF therapy or concomitant methotrexate (MTX) use in the FUTURE 5 study.

MATERIALS/METHODS: Adults (n=996) with active PsA, stratified by prior anti–TNF therapy (naive and inadequate response/intolerance [IR]) were randomized 2:2:2:3 to s.c. secukinumab 300 mg with loading dose (LD), 150 mg LD, 150 mg no LD, or placebo (PBO) at baseline (BL), Weeks 1, 2, 3, 4, and every 4 weeks thereafter.1 At Week 16, placebo non-responders were switched to secukinumab 300 or 150 mg. Concomitant methotrexate (≤25 mg/week) was allowed. Radiographic progression (mean change in van der Heijde-modified Total Sharp Score for PsA [vdH-mTSS] and its components: erosion and JSN scores from baseline to Week 24) was based on hand/wrist/foot X-rays obtained at baseline, Weeks 16 (non-responders) and Week 24, assessed by two blinded readers (plus an adjudicator if required). Average scores were used. Statistical analyses used linear extrapolation at Week 24 for all placebo non-responders and for all other patients with missing Week 24 X-rays.

RESULTS: At baseline, 30% of patients were anti–TNF-IR and 50% were on concomitant methotrexate. Radiographic progression was significantly inhibited at Week 24 in the overall population with secukinumab vs. placebo; mean change from baseline in vdH-mTSS was 0.08 (300 mg; $p<0.01$), 0.17 (150 mg; $p<0.05$), –0.09 (150 mg no LD; $p<0.01$) vs. 0.50 (placebo). Lower radiographic progression (vdH-mTSS, erosion, and JSN scores) was observed with secukinumab vs. placebo regardless of prior anti–TNF therapy or concomitant methotrexate use (Table 1).

CONCLUSIONS: Subcutaneous secukinumab 300 mg with loading dose, and 150 mg with and without loading dose, inhibited radiographic progression in patients with active PsA. Low rates of radiographic progression were observed regardless of previous anti–TNF therapy or concomitant methotrexate use.

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PA-51: Sustained and Improved Efficacy of Tildrakizumab from Week 28 to Week 52 in Treating Moderate-to-Severe Plaque Psoriasis

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BACKGROUND: Two phase-3, double-blind, randomized controlled trials (reSURFACE 1: NCT01722331; reSURFACE 2: NCT01729754) have demonstrated efficacy and safety of tildrakizumab, a high affinity, humanized, IgG1 κ, anti-interleukin–23 monoclonal antibody, in the treatment of adult patients with moderate-to-severe plaque psoriasis over 28 weeks. This analysis evaluated longer-term data from these two trials to examine whether the efficacy is sustained or improved from week 28 through week 52.

MATERIALS/METHODS: Both trials randomized adult patients with moderate-to-severe plaque psoriasis to receive tildrakizumab 100 mg or 200 mg at weeks 0, 4, then every 12 weeks. At week 28, patients with Psoriasis Area and Severity Index (PASI) response ≥50% were re-randomized, based on their week-28 PASI response, to receive the same, a higher or a lower dose of tildrakizumab or placebo (randomized withdrawal in reSURFACE 1 per the trial designs). The current analysis evaluated only patients treated with the same dose of tildrakizumab (100 mg or 200 mg) throughout the first 52 weeks. Four mutually exclusive groups were created based on week-28 PASI response: PASI 100, PASI 90-99, PASI 75-89 and PASI 50-74. PASI responses at week 52 (observed data) were analyzed for each week-28 PASI-response group.

RESULTS: This analysis included 352 patients on tildrakizumab 100 mg and 313 on tildrakizumab 200 mg. The proportions of patients achieving PASI 100, PASI 90-99, PASI 75-89 and PASI 50-74 at week 28 were 25.9%, 38.4%, 25.3% and 10.5% respectively for those on the 100 mg dose, and 24.6%, 24.3%, 19.5% and 31.6% respectively for those on the 200 mg dose. Among patients

who achieved week-28 PASI≥90 with either dose of tildrakizumab, 88.9-89.4% maintained PASI≥90 at week 52. Overall, 91.1% patients on the 100 mg dose and 93.9% on the 200 mg dose with week-28 PASI≥75 maintained PASI≥75 at week 52. Additionally, 39.3-40.4% of patients with week-28 PASI 75-89 remained PASI 75-89 at week 52 and 33.7%-41.0% improved to PASI≥90. Among patients with week-28 PASI 50-74, 20.2-29.7% achieved PASI≥90 and 52.5-64.9% achieved PASI≥75 at week 52. Overall, only 2.6% of patients on the 100 mg or 200 mg dose had week-52 PASI<50.

CONCLUSIONS: Among patients with moderate-to-severe plaque psoriasis treated with tildrakizumab 100 or 200 mg at weeks 0, 4, then every 12 weeks, those who achieved week-28 PASI≥50 and continued on the same dose had sustained or improved efficacy from week 28 through week 52. The majority patients who achieved week-28 PASI≥75 or PASI≥90 maintained PASI≥75 or PASI≥90 at week 52. Over half of week-28 partial responders (PASI 50-74) eventually achieved PASI≥75 and at least 1 in 5 achieved PASI≥90 at week 52.

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DISCLOSURES: Drs. Elewski, Menter, Crowley, Tyring and Gordon are the clinical investigators of the studies sponsored by Merck & Co., Inc., and Sun Pharmaceutical Industries, Inc. Drs. Zhao, Lowry, Rozzo and Mendelsohn and Mr. Parno are the employees of Sun Pharmaceutical Industries, Inc.

PA-52: Tildrakizumab Efficacy over Time by Week 28 Response Levels in Two Phase 3 Clinical Trials in Patients with Chronic Plaque Psoriasis

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BACKGROUND: Tildrakizumab (TIL), a high affinity, humanized, IgG1/κ monoclonal antibody for IL-23p19, recently demonstrated efficacy in patients with chronic plaque psoriasis in two, phase 3 clinical trials.

OBJECTIVE: To examine efficacy from baseline to week 52 among TIL patients achieving various Psoriasis Area and Severity Index (PASI) responses at week 28.

MATERIALS/METHODS: ReSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754) were double-blind, randomized controlled trials in subjects with moderate-to-severe chronic plaque psoriasis. Part 1 (0-12 weeks) was placebo controlled; Part 2 (12-28 weeks) re-randomized placebo patients to TIL; Part 3 (28-64 weeks, reSURFACE 1; 28-52 weeks, reSURFACE 2) patients with PASI ≥50 were re-randomized to continue or increase TIL dose or to placebo based on response at week 28. In this post-hoc pooled analysis, patients on TIL 100mg and 200mg from baseline to week 52 were classified in 5 mutually exclusive groups based on their week-28 PASI response: PASI <50, PASI 50-74, PASI 75-89, PASI 90-99, and PASI 100. Baseline characteristics and % PASI improvement from baseline up to week 52 (observed data) were examined for each group.

RESULTS: This analysis included 575 (TIL 100mg) and 581 (TIL 200 mg) patients. At week 28, 133 (23.1%), 175 (30.4%), 137 (23.8%), 82 (14.3%), and 48 (8.3%) TIL 100mg patients and 170 (29.3%), 169 (29.1%), 114 (19.6%), 105 (18.1%), and 23 (4.0%) TIL 200mg achieved PASI 100, PASI 90-99, PASI 75-89, PASI 50-74, and PASI <50, respectively. On average, PASI 100 patients were younger, lighter, and had shorter disease duration at baseline compared to other response groups. For TIL 100 mg, % PASI improvement was highest for PASI 100 and least for PASI<50 patients for all visits up to week 28 (week 4: 53%, 46%, 38%, 30%, and 16%; week 28: 100%, 95%, 83%, 64%, and 33% for PASI 100, PASI 90-99, PASI 75-89, PASI 50-74, and PASI <50 categories, respectively). Among patients achieving PASI >50 at week 28 and continued up to 52 weeks, % PASI improvement remained consistent or improved from week 28 to week 52. Similar results were observed for TIL 200mg as well as subgroup analysis with bio-naive and bio-experienced patients, respectively.

CONCLUSIONS: The majority of TIL 100 and 200 mg patients achieved PASI>50 response at week 28, and PASI improvement was maintained from week 28 to week 52. Among patients achieving ≥PASI 90 at week 28, TIL 100 and 200 mg were associated with rapid improvement by week 4.

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DISCLOSURES: Drs. Blauvelt, Sofen, Papp, Gooderham, and Reich are the clinical investigators of the study sponsored by Merck & Co., Inc., and Sun Pharmaceutical Industries, Inc. Drs. Zhao, Lowry, Rozzo and Mendelsohn and Mr. Parno are the employees of Sun Pharmaceutical Industries, Inc. Drs. Li, Cichanowitz, and Rosa are employees of Merck & Co., Inc.

PA-53: Time to Return of Disease Following Withdrawal from Brodalumab

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BACKGROUND: Brodalumab is a fully human anti–interleukin-17 receptor A (IL-17RA) monoclonal antibody that antagonizes inflammatory cytokines involved in psoriasis pathogenesis and is efficacious in treating moderate-to-severe plaque psoriasis.1 In the setting of a real-world clinical practice, it is relatively common for patients to stop and restart their medications because of a variety of factors.

OBJECTIVE: To present data on time to return of disease following

withdrawal from brodalumab.

MATERIALS/METHODS: In this phase 3, double-blind, placebo-controlled study (NCT01708590; AMAGINE-1), patients with moderate-to-severe psoriasis were randomized to brodalumab (140 or 210 mg) or placebo every 2 weeks (Q2W) during a 12-week induction phase.1 At week 12, patients receiving brodalumab who achieved a static physician's global assessment (sPGA) score of 0 or 1 were re-randomized to their induction dose of brodalumab or placebo. Time to loss of psoriasis area and severity index 50% improvement from baseline (PASI 50) was defined as the time from the end of treatment to loss of 50% of the week-12 PASI improvement. Time to return of disease was defined as an sPGA score ≥3. This study evaluated patients who received brodalumab 210 mg Q2W during the induction phase and who were randomized to receive placebo starting at week 12.

RESULTS: Of patients who received brodalumab 210 mg Q2W during the induction phase and were randomized to receive placebo starting at week 12 (n=84), time to loss of PASI 50 and time to return of disease were comparable across groups regardless of skin clearance response achieved at week 12. Of patients who achieved PASI 75 (n=84), PASI 90 (n=76), and PASI 100 (n=46) at week 12, mean (standard deviation) time to loss of PASI 50 following withdrawal from brodalumab was 72.0 (45.6), 72.3 (46.5), and 72.3 (44.4) days, respectively. For these same patients, mean (standard deviation) time to return of disease (sPGA score ≥3) following withdrawal from brodalumab was 74.7 (50.5), 72.6 (50.4), and 77.1 (53.1) days for patients who achieved PASI 75, PASI 90, and PASI 100 at week 12, respectively.

CONCLUSIONS: For patients with psoriasis who underwent abrupt treatment withdrawal in a clinical study of brodalumab, time to return of disease was consistent across patient groups regardless of response achieved at week 12. These findings provide guidance for clinical use of brodalumab for physicians to consider when planning treatment.

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