PA-01: A dose-finding clinical study with ingenol mebutate for field treatment of actinic keratosis on 250 cm² on trunk and extremities

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BACKGROUND: Ingenol mebutate (IngMeb) is approved for the field treatment of actinic keratosis (AK) in areas up to 25 cm².

OBJECTIVE: This phase 2, dose-ranging clinical study investigated the efficacy and safety of IngMeb in larger areas on trunk and extremities in patients with AK (NCT01998984).

METHODS: Multicenter, randomized, double-blind, parallel-group, vehicle-controlled 8-week clinical study, investigating efficacy and safety of 0.06% IngMeb gel for larger areas applied as field treatment once daily for 2, 3, or 4 consecutive days (2D, 3D, 4D) to approximately 250 cm² on the trunk or extremities in patients with 5–20 clinically typical AKs in the treatment area. Six individual components of LSRs were assessed on a scale from 0 to 4, yielding a maximum composite score of 24. Efficacy was assessed by AK count on days 31 and 56. LSRs and adverse events were assessed on days 1, 5, 10, 17, 31, and 56. Photo-damage outcome was assessed at day 56. Patients completed a burning sensation diary (reported as ‘application-site burning’ adverse event) on all treatment days.

RESULTS: 224 patients (92 US; 132 AUS) were randomized. In each treatment group, at least 87% of patients completed all treatments. Median age was 68 years; 64% were men, all were white, 99% had Fitzpatrick skin type I–III, with lighter skin types in AU than in US. The median history of AK was 12 years (US 8 years; AU 17 years). Baseline mean AK count in the treatment area was 12.2 (US 10.4; AUS 13.5). In 88% of patients the treatment area was the arm. Complete clearance at week 8 was achieved in 12.7% (2D), 5.1% (3D), and 26.8% (4D) vs 0% (vehicle) of patients, with a substantial variation depending on country and baseline AK count. The reduction in AK count at week 8 compared to baseline was significantly (P < .001) greater than with vehicle: 63.0% (2D); 66.8% (3D); 73.6% (4D) vs 11.9% (vehicle) with a dose response trend. Global photo-damage outcome assessment showed improvement for 80% (2D), 86% (3D), 98% (4D) vs 9% (vehicle) of patients. The composite LSR score peaked at day 5 or 10 for 2D, and day 5 for 3D and 4D, declined and was minimal at week 4. The mean peak composite LSR score for the three active treatments was higher than for vehicle with a dose response trend: 8.8 (2D); 9.5 (3D); 12.4 (4D) vs 2.2 (vehicle). The 2D and 3D treatments were well tolerated; however, the 4D arm was not tolerated, and was stopped during the trial based on predefined termination criteria. The most common adverse drug reactions were application-site pain/burning (81.8%; 84.7%; 87.8% vs 4.9%) and application-site pruritus (34.5%; 45.8%; 28.6% vs 3.3%) in 2D, 3D, 4D, and vehicle groups, respectively.

LIMITATIONS: Phase 2 trial with limited amount of data.

CONCLUSION: The 2D and 3D treatments with 0.06% IngMeb gel for larger areas were well tolerated and effective in reducing the AK count in the treated field on trunk and extremities. The 4D treatment was effective but not tolerable.


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PA-02: A novel nonsteroidal, topical, anti-inflammatory, phosphodiesterase 4 inhibitor, crisaborole topical ointment, 2% reduces pruritus and signs of atopic dermatitis in two phase 3 studies in children and adults with mild-to-moderate atopic dermatitis

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BACKGROUND: Atopic dermatitis (AD) is an inflammatory skin disease that can present with intense pruritus and inflamed, red, weepy lesions. Crisaborole Topical Ointment, 2% (Anacor Pharmaceuticals, Palo Alto, CA) is an investigational, non-steroidal, topical, anti-inflammatory, phosphodiesterase 4 inhibitor being studied for the treatment of AD.

OBJECTIVE: To analyze the exploratory efficacy endpoints evaluating crisaborole’s impact on pruritus and signs of AD from 2 identical Phase 3 studies (NCT02118766 and NCT02118792).

METHODS: Two identically designed multicenter, double-blind, vehicle-controlled Phase 3 studies enrolled patients ≥2 years old with mild-to-moderate AD. Patients were randomized 2:1 to receive Crisaborole Topical Ointment, 2% or vehicle twice daily for 28 days. Exploratory efficacy endpoints were evaluated on a 4-point scale (None [0] to Severe [3]). The severity of pruritus was examined twice daily and time to success was determined by Kaplan-Meier analysis. Signs of AD (erythema, induration/ papulation, exudation, excoriation, and lichenification) were examined weekly. Success for each sign or symptom was defined as achievement of None (0) or Mild (1) pruritus with ≥1-grade improvement from baseline.

RESULTS: Enrollment of crisaborole:vehicle patients was 503:256 and 513:250 for Study 1 and Study 2, respectively. Baseline severity of symptoms and signs were generally balanced across treatment groups/studies. Crisaborole-treated patients achieved success in pruritus earlier than vehicle-treated patients (pooled data: median 1.37 vs 1.70 days; P = .001). In both studies, a greater proportion of crisaborole-treated patients achieved success than vehicle-treated patients for all clinical signs of AD by Day 29 (study 1 crisaborole vs vehicle; study 2 crisaborole vs vehicle) (erythema: 62.8% vs 46.1%; 54.9% vs 33.9%; induration/papulation 57.7% vs 54.8%; 51.9% vs 40.2%; exudation 41.0% vs 33.3%; 38.1% vs 27.2%; excoriation 63.0% vs 51.8%; 57.2% vs 44.2%; lichenification 51.7% vs 46.5%; 51.4% vs 35.3%).

LIMITATIONS: Pruritus and signs of AD were exploratory endpoints; thus, the study was not powered to detect a difference in these measures.

CONCLUSION: Crisaborole Topical Ointment, 2% may represent a safe and efficacious treatment for patients as young as 2 years with mild-to-moderate AD, as demonstrated by early relief of pruritus and improvement in signs of AD in two large phase 3 studies.

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DISCLOSURES: AA HEBERT reports grants and other from ANACOR, during the conduct of the study; grants and other from ANACOR, outside the submitted work. LF Eichenfield reports grants and personal fees from Anacor, during the conduct of the study; personal fees from Anacor, outside the submitted work. MG Lebwohl reports other from Amgen, other from Anacor, other from Aqua, from Canfile Biopharma, from Celgene, from Clinuvel, from Coronado, from Biosciences, from Ferdendale, from Lilly, from Janssen Biotech, from Leo Pharmaceuticals, from Merz, from Novartis, from Pfizer, from Sandoz, from Valeant, outside the submitted work. AS Paller reports personal fees from Anacor, during the conduct of the study. EL Simpson reports other from Regeneron, other from Guidedepoint Global, other from ClearView Healthcare, other from MedImmune, other from Galderma, other from Genentech, other from Anacor, during the conduct of the study; personal fees from Valeant, personal fees from Pfizer, other from Regeneron, other from MedImmune, other from Galderma, other from Genentech, other from Pfizer, other from Merck, other from Valeant, other from Chugai, other from Otsuka, other from Amgen, other from Tioga, personal fees from Brown University, outside the submitted work. WL Dr. Tom reports other from Anacor, Inc, during the conduct of the study. MH Hughes has nothing to disclose. LT Zane reports personal fees from Anacor, outside the submitted work.

PA-03: A phase 3 trial comparing ixekizumab with placebo and etanercept for moderate-to-severe plaque psoriasis; results from the 12-week induction period of UNCOVER-2


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BACKGROUND: IL-17A plays a key role in the immunopathogenesis of psoriasis.

OBJECTIVE: To evaluate the efficacy and safety of an anti-IL-17A monoclonal antibody, ixekizumab, for the treatment of psoriasis.

METHODS: In this double-blind trial, 1,224 patients were randomized to receive subcutaneous placebo (n = 168), etanercept (50 mg twice weekly; n = 358), or a single injection of 80 mg ixekizumab every 2 (IXE Q2W; n = 351) or 4 weeks (IXE Q4W;
n = 347) following a 160 mg starting dose. The co-primary efficacy endpoints were proportions of patients who achieved 1) an sPGA 0/1, and 2) PASI 75 by Week 12. Treatment groups were compared using the Cochran-Mantel-Haenszel test. For response analyses, missing data were imputed using non-responder imputation.¹

RESULTS: At Week 12, PASI 75 response rates were 89.7% in IXE Q2W, 77.5% in IXE Q4W, 2.4% in placebo, and 41.3% in etanercept groups, and sPGA 0/1 was achieved by 83.2% in the IXE Q2W, 72.9% in IXE Q4W, 2.4% in placebo, and 36.0% in etanercept groups (P < .001 each ixekizumab vs placebo or etanercept). Differences were seen as early as Week 1 for IXE Q2W and IXE Q4W compared to the etanercept group (P < .05). Complete resolution (PASI 100) was achieved 40.5% in IXE Q2W, 30.8% in IXE Q4W, 0.6% in placebo, and 5.3% in etanercept groups (P < .001 each ixekizumab vs placebo or etanercept). Treatment-emergent adverse events reported in ≥5% of ixekizumab-treated patients and at higher percentages than in placebo-treated patients included injection-site reaction and headache, most of which were mild to moderate in severity. The percentages of these events in ixekizumab-treated patients were similar to those in etanercept-treated patients. Serious adverse events were reported in 1.4% of IXE Q2W, 1.7% of IXE Q4W, 1.2% of placebo, and 1.7% of etanercept patients.

LIMITATIONS: A limitation is the relatively short duration of the trial.

CONCLUSIONS: Both ixekizumab dosing regimens were highly effective and superior to placebo and etanercept with onset of efficacy as early as Week 1 and a safety profile comparable to etanercept in this induction period. Over 75% of ixekizumab-treated patients achieved PASI 75, and over 30% achieved complete resolution of psoriasis.

DISCLOSURES: CE Griffiths receives grant/research support from Abbott, Janssen, Celgene, Eli Lilly and Company, MSD, Bristol-Myers Squibb, Novartis, Sandoz, LEO, Trident, Regeneron, Pfizer; and is a consultant of AbbVie, Actelion, Janssen, Amgen, Eli Lilly and Company, Celgene, Pfizer, Sandoz, UCB Pharma, GSK-Stiefel, and LEO. K Reich is a consultant of AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, and Xenoprot; and is a member of the speakers bureau of AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, and Xenoprot. M Lebwohl received grant/research support from AbGenomics, Amgen, Anacor, Canfite Biopharma, Celgene, Clinuvel, Corazono Biosciences, and Ferndale; and is a consultant of Dermispor. P Van de Kerkhof is a consultant of Celgene, Centocor, Allmiral, Amgen, Pfizer, Phillips, Abbott, Eli Lilly and Company, Galderma, Novartis, Janssen Cilag, LEO Pharma, Sandoz, and Mitsuishi. C Paul receives grant/research support from Pierre Fabre; and is a consultant of Pfizer, AbbVie, Amgen, Celgene, Janssen, Eli Lilly and Company, LEO, Novartis, and GSK. A Menter receives grant/research support from AbbVie, Allergan, Amgen, APOPharma, Boehringer Ingelheim, Cengene, Convoy Therapeutics, Eli Lilly and Company, Genentech, Janssen Biotech, Leo Pharma, Merck, Novartis, Pfizer, Symbio, Syntryx, Wyeth, and XenoPort; is a consultant of AbbVie, Allergan, Amgen, Convoy Therapeutics, Eli Lilly and Company, Janssen Biotech, Novartis, Pfizer, Syntryx, Wyeth, and XenoPort; and is a member of the speakers bureau of AbbVie, Amgen, Janssen Biotech, Leo Pharma, and Wyeth. K Papp receives grant/research support from Abbott, Amgen, Anacor, Astellas, Celgene, Celtic, Dow Pharma, Eli Lilly and Company, Galderma; is a consultant of Abbott, Akesis, 3M, Akros, Alza, Amgen, Astellas, Baxter, Boehringer Ingelheim, Celgene, Centocor, Cipher, Eli Lilly and Company, Forward Pharma, Funxional Therapeutics; and is a member of the speakers bureau of Abbott, 3M, Amgen, and Astellas. K Solotkin (Presenter) LY, G Cameron, J Erickson, L Zhang, R Secret, S Ball, O Osuntokun, D Braun, and B Nicholson are employees and shareholders of Eli Lilly and Company. M Heffernan is a shareholder and consultant of Eli Lilly and Company.

FUNDING: Sponsored by Eli Lilly and Company.


PA-04: A phase 3 trial comparing ixekizumab with placebo and etanercept for moderate-to-severe plaque psoriasis: results from the 12-week induction period of UNCOVER-3


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BACKGROUND: IL-17A plays an important role in the immunopathogenesis of psoriasis.

OBJECTIVE: To assess the efficacy and safety of an anti-IL-17A monoclonal antibody, ixekizumab, for the treatment of psoriasis.

METHODS: In this double-blind trial, 1,346 patients were ran-
domized to receive subcutaneous placebo (n = 193), etanercept (50 mg twice weekly; n = 382), or a single injection of 80 mg ixekizumab every 2 (IXE Q2W; n = 385) or 4 weeks (IXE Q4W; n = 386) following a 160 mg starting dose. The co-primary efficacy endpoints were proportions of patients who achieved 1) an sPGA 0/1, and 2) PASI 75 at Week 12. Treatment groups were compared using the Cochran-Mantel-Haenszel test. For response analyses, missing data were imputed using nonresponse imputation (NRI).1

RESULTS: At Week 12, PASI 75 response rates were 87.3% in IXE Q2W, 84.2% in IXE Q4W, 7.3% in the placebo, and 53.4% in etanercept groups, and sPGA 0/1 was achieved by 80.5% in IXE Q2W, 75.4% in IXE Q4W, 6.7% in placebo, and 41.6% in etanercept groups (P < .001 each ixekizumab vs placebo or etanercept). Differences were seen as early as Week 1 for IXE Q2W and IXE Q4W compared to the etanercept group (P < .05). Complete resolution (PASI 100) was achieved by 37.7% in IXE Q2W, 35.0% in IXE Q4W, 0 in placebo, and 7.3% in etanercept groups (P < .001 each ixekizumab vs. placebo or etanercept).

Treatment-emergent adverse events reported in ≥5% of all ixekizumab patients and at higher percentages than in placebo patients included injection-site reaction and nasopharyngitis. Most of these events were mild to moderate in severity. The percentages of these events in ixekizumab patients were similar to those in etanercept patients. Serious adverse events were reported in 2.3% of IXE Q2W, 1.6% of IXE Q4W, 2.6% of placebo, and 1.3% of etanercept patients.

LIMITATIONS: A limitation is the relatively short duration of the trial.

CONCLUSIONS: Both ixekizumab dosing regimens were highly effective and superior to placebo and etanercept with onset of efficacy as early as Week 1 and a safety profile comparable to etanercept in this induction period. Over 80% of ixekizumab-treated patients achieved PASI 75, and over 35% achieved complete resolution of psoriasis.

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DISCLOSURES: CE Griffiths receives grant/research support from AbbVie, Janssen, Celgene, Eli Lilly and Company, MSD, Bristol-Myers Squibb, Novartis, Sandoz, LEO, Trident, Regeneron; and is a consultant of AbbVie, Actelion, Janssen, Amgen, Eli Lilly and Company, Celgene, Pfizer, Sandoz, UCB Pharma, GSK-Stiefel, and LEO. K Reich is a consultant of AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, Xenoprot; and is a member of the speakers bureau of AbbVie, Janssen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, and Xenoprot. M Lebwohl receives grant/research support from AbGenomics, Amgen, Anacor, Canfite Biopharma, Celgene, Clinuvel, Corazono Biosciences, Fendale; and is a consultant of Dermipsor. P Van de Kerkhof is a consultant of Celgene, Centocor, Allmirall, Amgen, Pfizer, Phillips, Abbott, Eli Lilly and Company, Galderma, Novartis, Janssen, Cilag, Leo Pharma, Mitsubishi, and Sandoz. C Paul receives grant/research support from Pienne Fabre; and is consultant of Pfizer, AbbVie, Amgen, Celgene, Janssen, Eli Lilly and Company, Leo, Novartis, and GSK. A Menter receives grant/research support from AbbVie, Allergan, Amgen, APoPharma, Boehringer Ingelheim, Cengene, Convoy Therapeutics, Eli Lilly and Company, Genentech, Janssen Biotech, Leo Pharma, Merck, Novartis, Pfizer, Symbio, Syntryx, Wyeth, and Xenoprot; is a consultant of AbbVie, Allergan, Amgen, Convoy Therapeutics, Eli Lilly and Company, Janssen Biotech, Novartis, Pfizer, Syntryx, Wyeth, Xenoprot, and a member of the speakers bureau of AbbVie, Amgen, Janssen Biotech, Leo Pharma, and Wyeth. K Solotkin (Presenter), G Cameron, J Erickson, L Zhang, R Secret, S Ball, O Osutokun, D Braun, and B Nickoloff are employees and shareholders of Eli Lilly and Company. M Heffernan is a shareholder of Eli Lilly and Company; and a consultant of Eli Lilly and Company. K Papp receives grant/research support from Abbott, Amgen, Anacor, Astellas, Celgene, Celtic, Dow Pharma, Eli Lilly and Company, and Galderma; is a consultant of Abbott, 3M, Akesis, Allergan, Alza, Amgen, Astellas, Baxter, Boehringer Ingelheim, Celgene, Centocor, Cipher, Eli Lilly and Company, Forward Pharma, and Funxional Therapeutics; and is a member of the speakers bureau of Abbott, Akesis, Amgen, and Astellas.

FUNDING: Sponsored by Eli Lilly and Company.


PA-05: An in vitro study demonstrating nail penetration of tavaborole from tavaborole topical solution, 5% through multiple layers of nail polish

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BACKGROUND: Onychomycosis is a common infection of the fingernails and toenails resulting in thickening, discoloration, and deformity of the nail plate. Onychomycosis may have a significant psychological impact on individuals affected by this condition. Tavaborole Topical Solution, 5% (tavaborole; Anacor Pharmaceuticals, Inc, Palo Alto, CA) is a novel, boron-based pharmaceutical approved by the US FDA in July 2014 for the treatment of toenail onychomycosis caused by Trichophyton rubrum and T. mentagrophytes. 1) It is a highly specific protein synthesis inhibitor that targets fungal cytoplasmic leucyl-tRNA synthetase (LeuRS), an aminoacyl-tRNA synthetase. These enzymes play a pivotal role in maintaining and translating the genetic code within DNA. 2) Tavaborole binds to the active editing site and traps tRNA, preventing catalytic turnover and...
synthesis of leucine-charged tRNAs. In this way, tavaborole inhibits cellular protein synthesis and suppresses fungal activity.

3) Tavaborole retains its pharmacologic activity in the presence of keratin remaining in the nail plate for at least 3 months after dosing.

**OBJECTIVE:** The objective of this study was to evaluate the nail penetration properties of Tavaborole Topical Solution, 5% through multiple layers of nail polish.

**METHODS:** Human cadaver fingernails from eight female donors were mounted on Vertical Diffusion Cells and randomized to four groups representing different nail polish application practices (for each, N=7); Tavaborole Topical Solution, 5% was applied daily (25 μL/cm²) to each nail for 14 days. The groups were as follows: Group 1: 4 coats of Salon Typical (1 base coat, 2 coats of polish, 1 clear coat); Group 2: 1 coat of a Salon Typical; Group 3: 2 coats of a home typical; Group 4: 1 coat of a home typical; and a unpainted reference control.

**RESULTS:** Mean (standard deviation) cumulative penetration of tavaborole from Tavaborole Topical Solution, 5% through nails after 14 days of dosing: Group 1: 1178.53 (554.40); Group 2: 1227.30 (974.00); Group 3: 1492.52 (1322.09); Group 4: 1428.19 (840.82); unpainted nails: 565.91. Nail penetration was measured by monitoring the rate of drug appearance each day in the receiving medium. Approximately 24 hours after each dose, the receiving medium from each cell was removed and replaced with fresh solution. Prior to each subsequent daily dose, the nails were cleaned with a cotton swab moistened with water. Aliquots of each receiving medium sample were analyzed using high performance liquid chromatography.

**CONCLUSION:** Tavaborole Topical Solution, 5% can penetrate through up to four layers of nail polish.

**DISCLOSURES:** BE Elewski reports other from Pfizer, other from Novartis, other from Valeant, other from Eli Lilly, other from Amgen, other from Celgene, other from Janssen, other from Regeneron, other from Viamet, outside the submitted work. P Rich is an investigator for Novartis. D Coronado has a patent Compounds and Nail Polish pending. S Chanda has no disclosures. T Merchant has a patent Compounds and Nail Polish pending. S Chanda has no disclosures. LT Zane is a salaried employee of Anacor and reports personal fees from Anacor, outside the submitted work. T Vlahovic reports other from Pharmaderm, other from valeant, outside the submitted work.

**PA-06: Biologic therapy persistence in psoriatic disease in the psoriasis longitudinal assessment and registry (PSOLAR)**


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**BACKGROUND:** To look at persistency of biologic therapy in pts with psoriasis and psoriatic arthritis using data from the PSOLAR registry.

**OBJECTIVE:** We describe persistency of biologic use in pts with psoriasis (PsO) and psoriatic arthritis (PsA) in PSOLAR.

**METHODS:** PSOLAR evaluates outcomes for PsO pts eligible to receive treatment with systemic agents. Among PSOLAR pts, 36% (n = 4,317) have self-reported PsA. Duration of therapy was defined as time (days) between first dose of biologic and first of: 1) discontinuation, 2) switch, 3) registry withdrawal, or 4) last data cut (August 23, 2013). Separate analyses were performed for: 1st line (bio-naïve), 2nd line, and 3rd line usage to reduce confounding associated with prior exposures for the overall and PsA populations. Persistence was assessed by Kaplan-Meier analysis for time to therapy stop/switch separately for ustekinumab(UST), infliximab(IFX), adalimumab(ADA), and etanercept(ETN). Cox proportional hazard regression analysis compared time to stop/switch of UST with other biologics for each cohort.

**RESULTS:** Most starts were attributed to UST(1833 pts) and ADA(1303) with fewer starts for ETN(537) and IFX(327). Among UST starts, the proportions of 1st, 2nd and 3rd line usage were 20%, 31%, and 30%; ADA starts 31%, 48%, and 15%; ETN starts 54%, 29% and 13%; IFX starts 19%, 28% and 32%, respectively. Baseline clinical characteristics were generally comparable across biologics and cohorts. Fewer pts discontinued UST than IFX, ETN, and ADA in all 3 lines. Median duration of therapy was generally longer for UST vs anti-TNF therapies. For 1st line starts, better persistence was observed for UST based on significant differences in time to stop/switch for each biologic vs UST (IFX vs UST: HR, 3.04; CI,1.66-5.57; P < .0003; ADA vs UST: HR, 4.99; CI, 3.39-7.35; P < .0001; ETN vs UST: HR, 5.59; CI,3.77-8.29; P < .0001). Similar results were observed for 2nd and 3rd line starts. In the subgroup with self-reported PsA, for 1st line starts, better persistence was observed with UST vs ETN (HR, 2.53; CI, 1.39-4.62; P = .0024); no significant differences were seen for UST vs IFX and ADA. UST had better persistence vs anti-TNFs in the analyses of 2nd and 3rd line starts. Reasons for stop/switch were similar across biologics and cohorts.

**LIMITATIONS:** Data were not adjusted for differences among cohorts, eg, MTX use, insurance, administration setting, and region.

**CONCLUSION:** Persistence of UST therapy in psoriatic disease was significantly better than anti-TNF therapies in biologic-naïve and experienced pts, with lower rates of stopping/switching and higher median days on therapy.

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PA-07: BPX-01: in vivo delivery and safety of minocycline topical gel

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BACKGROUND: Acne vulgaris is a chronic skin disorder that occurs in teens and adults. Acne is a multifactorial inflammatory disease and presents itself as comedones, papules and pustules, and in some cases results in scarring. The pathogenesis of acne involves an increase in sebum production, follicular hyperkeratinization, Propionibacterium acnes (P. acnes) colonization, and inflammation. Treatments do exist that can reduce the number of P. acnes, but such treatments often have been associated with the emergence of resistance in P. acnes. Oral treatments can be used, alone or in combination with topical products.

OBJECTIVE: The disorder affects children as young as 9 years of age. A need exists not only to provide an effective therapy, but also a treatment that minimizes exposure of young children to excessive amount of drug. Newer treatment vehicles are needed that ensure stability and better delivery of the active pharmaceutical ingredient (API) for effective management of acne.

METHODS: Recently, a unique, stable, hydrophilic topical gel formulation BPX-01 was developed for the treatment of acne vulgaris. In our previous in vitro penetration studies, we have compared a low dose API formulation (BPX-01) to a high dose alternate formulation. In this report, we further present results from our in vivo penetration studies performed in minipigs and rats to evaluate the absorption of BPX-01 in skin.

RESULTS: Our studies indicate local delivery of the API into the epidermis and sebaceous glands in vivo. BPX-01 application is a simple topical gel. It distributes evenly, is not sticky and does not occlude the skin.

CONCLUSION: These studies have demonstrated efficient delivery into the skin with no irritation, suggesting that BPX-01 could be useful to successfully treat acne.

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DISCLOSURES: GS Herron reports other from BioPharmX, Inc, during the conduct of the study. D Lac reports other from BioPharmX, Inc, during the conduct of the study; in addition D Lac has a patent pharmaceutical tetracycline composition for dermatological use pending to BioPharmX, Inc. M Hermsmeier reports other from BioPharmX, Inc, during the conduct of this study. SY Huang reports other from BioPharmX, Inc, during the conduct of the study. X Chen, N Yam, and A Yamamoto, reports other from BioPharmX, Inc, during the conduct of the study; in addition they have a patent pharmaceutical tetracycline composition for dermatological use pending to BioPharmX, Inc. KF Chan and U Nagavarapu report other from BioPharmX, Inc, during the conduct of the study.

PA-08: Complete resolution of psoriasis is associated with greater improvements in itch and health-related quality of life: an analysis from UNCOVER-2, a phase 3 clinical trial of IXEKIZUMAB

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BACKGROUND: Psoriasis has serious impacts on health-related quality of life (HRQoL), and itch is an important symptom for many patients. Currently, PASI 75 is considered a good treatment goal for psoriasis patients; however, individuals not achieving complete resolution of psoriatic lesions (ie, PASI 100) may have continued impairment in HRQoL.

OBJECTIVE: To evaluate differences in patient reported outcomes (PROs) among individuals who achieve PASI 100 compared to those with lower treatment responses in patients with psoriasis participating in a trial of ixekizumab, an anti-IL-17A monoclonal antibody.

METHODS: In this trial, 1,224 patients were randomized to receive subcutaneous placebo, etanercept (50 mg twice weekly), or a single injection of 80 mg ixekizumab every 2 or 4 weeks following a starting dose of 160 mg. Treatment groups were combined for the analyses. PROs included the Itch Numeric Rating Scale (Itch NRS), which ranges from 0 to 10 (no itch to severe itch), and the DLQI (scores of 0–1 are interpreted as disease having no effect at all on a patient’s life). Improvements in PROs at Week 12 were compared pairwise between groups of patients achieving <50% improvement in PASI (PASI <50 [n = 354]), 50%–75% improvement in PASI (PASI 50–<75 [n = 134]), 75%–90% improvement in PASI (PASI 75–<90 [n = 213]), 90%–100% improvement in PASI (PASI 90–<100 [n = 254]), and 100% improvement in PASI (PASI 100 [n = 269]).

RESULTS: Greater improvements in DLQI and Itch NRS were associated with greater improvements in psoriasis with maximum improvements in the PASI 100 group (P < .01 for all pairwise comparisons between subgroups). In the PASI 100 group, there were significantly greater reductions in Itch NRS (-5.9 vs -4.6, respectively; P < .01) and more patients with a DLQI score of 0 or 1 (78% vs 53%, respectively; P < .01) compared to the PASI 75–<90 group.

LIMITATIONS: Results are limited to the 12 week induction period of this trial.
CONCLUSIONS: Maximum reductions in itching and the highest percentage of patients reporting no impact of psoriasis on HRQoL were observed among those who achieved complete resolution of psoriasis compared to those achieving lower levels of response suggesting that clear skin is a desirable treatment goal for patients.  
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DISCLOSURES: CE Griffiths has received Grant/Research support from AbbVie, Janssen, Celgene, Eli Lilly and Company, MSD, Bristol-Myers Squibb, Novartis, Sandoz, LEO, Trident, Regeneron, and Pfizer; and is a consultant of AbbVie, Actelion, Janssen, Amgen, Eli Lilly and Company, Celgene, Pfizer, Sandoz, UCB Pharma, GSK-Stiefel, LEO. A Blauvelt is a consultant of AbbVie, Amgen, Boehringer Ingelheim, Celgene, and Janssen. M Lebwohl has received Grant/Research support from AbGenomics, Amgen, Anacor, Canfiite Biopharma, Celgene, Clinuvel, Coronado Biosciences, Ferndale; and is a consultant of Dermipsor. K Reich is a consultant of AbbVie, Amgen, Biogen-Idec, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, and Xenoprot; and is on the speakers board for ABBVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly and Company, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, MSD, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB, Vertex, Xenoprot. K Solotki (Presenter), E Nikai, and O Goldblum are employees and stockholders of Eli Lilly and Company.

FUNDING: Sponsored by Eli Lilly and Company. are employees and shareholders of Eli Lilly and Company.

PA-09: Composite assessment of sonidegib efficacy in patients with labBCC using two sets of response criteria

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BACKGROUND: In the pivotal phase 2 BOLT study (NCT01327053; Migden et al. Lancet Oncol. 2015), durable responses were observed in patients with advanced BCC treated with sonidegib, a hedgehog pathway inhibitor (HPI). In the BOLT trial, treatment responses were assessed using modified RECIST criteria—a composite evaluation more stringent than standard RECIST criteria used in prior studies of HPIs in BCC.

OBJECTIVE: In this analysis, treatment responses in BOLT were evaluated using two different sets of criteria: mRECIST (A; used in BOLT) and mRECIST-like (B; similar to criteria used in other HPI studies, with less stringent requirements for complete response [CR]).

METHODS: Assessments by MRI per RECIST v1.1, photography per WHO guidelines, and histology in multiple biopsies were used to determine a composite overall response (COR) in patients with locally advanced basal cell carcinoma (labBCC) treated with sonidegib 200 mg once daily (QD) using criteria A and B. The main distinction between A and B was the level of stringency required to achieve a COR of CR. Criteria B allowed a COR of CR when there was any response (CR or PR) by MRI or photography, as long as the histology result was negative; in contrast, in the same cases, a COR per criteria A required CR (or CR equivalent) for all image modalities used and negative histology. Objective response rate (ORR), best overall response (BOR), and disease control rate (DCR; CR + PR + SD) were assessed by central review using both criteria (12-mo data; cutoff: Dec 31, 2013; median follow-up: 20 mo).

RESULTS: The ORR and DCR were similar with both criteria, but the CR rate was higher with criteria B than with A (20% vs 5%). Efficacy of sonidegib 200 mg QD in patients with labBCC: criteria A vs B (all %; n=66): ORR: 58 vs 62 (95% CI 45-70 vs 49-74); BOR: 5 vs 20; PR: 53 vs 42; SD: 33 vs 29; Progressive disease: 2 vs 2; Unknown: 8 vs 8; DCR: 91 vs 91.

CONCLUSION: These data demonstrate a high response to sonidegib and the stringency of the BCC-mRECIST criteria used in BOLT. The higher CR rate with the mRECIST-like criteria observed in this analysis was due to the less stringent requirement for a COR of CR (ie, negative histology could overrule MRI/photography data that indicate residual disease). Despite the inherent challenges of assessing tumor response in labBCC, both evaluation criteria support the clinical benefit of sonidegib in this difficult-to-treat patient population.

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DISCLOSURES: R Dummer reports grants and personal fees from Novartis during the conduct of the study; grants and personal fees from Bristol-Myers Squibb, grants and personal fees from Roche, grants and personal fees from GlaxoSmithKline, personal fees from Merck Sharp & Dhome, personal fees from Amgen, outside the submitted work. J. Grichnik served as a consultant to Novartis during the study; he has also served as a consultant for Amgen, Castle Biosciences, and caliber Imaging & Diagnostics, Inc. He is also a founder and major shareholder in DigitalDerm, Inc. L Schwartz reports other from Novartis, during the conduct of the study; personal fees from Pfizer, other from BioClinica, other from Celgene, other from ICON Clinical Research, outside the submitted work. S Gogov is an employee of Novartis Pharmaceuticals AG. T Yi, M Mone and D Sellami are employees of Novartis Pharmaceuticals Corporation. M Migden acted as an advisor for Novartis, Genentech, Lilly.
**PA-10: Consistent high efficacy adalimumab PASI75 responders: a post hoc analysis of REVEAL**

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**BACKGROUND:** Phase 2/3 clinical trials of adalimumab (ADA) in patients with moderate to severe psoriasis (Ps) have demonstrated that a high proportion of patients treated with ADA achieve a Psoriasis Area and Severity Index (PASI) 75 response. Among PASI75 responders at Week 33 of the REVEAL trial, PASI90/100 responses at Week 33 were 67% and 33%, respectively.1

**OBJECTIVE:** This post hoc analysis was conducted to assess, among patients treated with ADA who achieved a PASI75 response, whether this high-efficacy response was consistently maintained and affected other efficacy endpoints (eg, DLQI).

**METHODS:** REVEAL (NCT00237887) was a 52-week, double-blind, randomized, placebo (PBO)-controlled phase 3 study of ADA for moderate to severe plaque Ps. At Week 16, ADA-treated patients with ≥PASI75 response continued onto period B. Patients from the ADA arm of Period B with a ≥PASI75 response at Week 33, were rerandomized in Period C to continue ADA 40 mg eow or to receive PBO, and sustained responses were assessed at Week 52. Patients were considered to have a consistent high-efficacy response if their PASI score at every visit after Week 33 until Week 52 was never >2 points higher than their Week 33 PASI score.

**RESULTS:** A total of 250 patients achieved a PASI75 response at Week 33 and were rerandomized to continue ADA treatment; 245 patients had a study visit after Week 33 and were evaluable for consistent high-efficacy response. A total of 76.3% of patients (187/245) were consistent high-efficacy responders through Week 52. PASI75/90/100 response rates after 52 weeks of continuous ADA treatment were 84%/58%/33%, respectively. The mean change from baseline in PASI scores among high-efficacy responders at Week 52 was −16.7 and was significantly greater than in patients without a consistent high-efficacy response (−14.5; \( P = .018 \)). Mean Dermatology Life Quality Index scores at Week 52 were 0.8 among high-efficacy responders compared with 4.3 among those without a consistent high-efficacy response. Of the ADA-treated patients with post-week 33 PASI data, 10 (6.0%) of the PASI90 responders and 1 (1.2%) of the PASI100 responders at re-rerandomization lost their PASI75 response by Week 52.

**CONCLUSION:** Evaluation of an enriched population of patients who had PASI75 response at Weeks 16 and 33 and after initiating ADA demonstrated that the majority of these patients had consistent high-efficacy response with continued ADA therapy beyond Week 33. Patients with consistent high-efficacy responses had better quality of life scores compared to those without consistent high-efficacy responses.

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**DISCLOSURES:** K Gordon received payment for work by commercial organisations either directly or indirectly through an intermediary: AbbVie, Amgen, Celgene, Eli Lilly, Jannsen, Novartis, and Pfizer. M Karunaratne and DA Williams receive a salary as employees of AbbVie and may also receive AbbVie stock, stock options and/or stock grants. M Okun is a former employee of AbbVie and is now affiliated with Fort HealthCare.

**FUNDING:** 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-11: Crisaborole topical ointment 2%, a novel nonsteroidal, topical, anti-inflammatory, phosphodiesterase 4 inhibitor: results in children and adults with mild-to-moderate atopic dermatitis from two phase 3 studies**

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**BACKGROUND:** To investigate the safety and efficacy of Crisaborole Topical Ointment, 2% in mild-to-moderate AD evalu-
CONCLUSION: To report cumulative incidence and results of analysis of malignancies excluding non-melanoma skin cancers (NMSC) in PSOLAR. METHODS: PSOLAR is a multicenter, longitudinal, observational study evaluating long-term safety and clinical outcomes for pts eligible to receive treatment for psoriasis with biologics and/or conventional systemic agents. The incidence of malignancies excluding NMSC (e.g. basal/squamous cell carcinomas) overall and by treatment is reported. The rules for attribution of a malignancy to a therapy use a definition of exposure based on whether pts had ever been exposed to a given therapy at any time prior to the event. In cases of exposure to >1 therapy, the rule for attribution of malignancy to a treatment is ustekinumab(UST) 1st, infliximab(IFX)/golimumab(GLM) 2nd, other biologics 3rd (nearly all adalimumab(ADA) or etanercept(ETN), or non-biologic therapy 4th, which is consistent with the pre-specified analytic plan. Analysis using Cox hazard regression was used to identify predictors of malignancy and included medication exposure defined as UST vs no biologic and biologics other than UST (primarily ADA, IFX and ETN) vs no biologic.

RESULTS: PSOLAR is fully enrolled and, as of Aug 23, 2013, has 31 818 total pt-years of follow up with 12,095 pts. Cumulative rates of malignancy overall and across treatments were:

**PA-12: Current status of observations of malignancies in the psoriasis longitudinal assessment and registry (PSOLAR) study**

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**BACKGROUND:** To look at the current rate of malignancy (excluding NMSC) occurrence in the PSOLAR registry. **OBJECTIVE:** To report cumulative incidence and results of analysis of malignancies excluding non-melanoma skin cancers (NMSC) in PSOLAR. **METHODS:** PSOLAR is a multicenter, longitudinal, observational study evaluating long-term safety and clinical outcomes for pts eligible to receive treatment for psoriasis with biologics and/or conventional systemic agents. The incidence of malignancies excluding NMSC (e.g. basal/squamous cell carcinomas) overall and by treatment is reported. The rules for attribution of a malignancy to a therapy use a definition of exposure based on whether pts had ever been exposed to a given therapy at any time prior to the event. In cases of exposure to >1 therapy, the rule for attribution of malignancy to a treatment is ustekinumab(UST) 1st, infliximab(IFX)/golimumab(GLM) 2nd, other biologics 3rd (nearly all adalimumab(ADA) or etanercept(ETN), or non-biologic therapy 4th, which is consistent with the pre-specified analytic plan. Analysis using Cox hazard regression was used to identify predictors of malignancy and included medication exposure defined as UST vs no biologic and biologics other than UST (primarily ADA, IFX and ETN) vs no biologic.

RESULTS: PSOLAR is fully enrolled and, as of Aug 23, 2013, has 31 818 total pt-years of follow up with 12,095 pts. Cumulative rates of malignancy overall and across treatments were:
**PA-13: DFD-01, a novel formulation of 0.05% betamethasone dipropionate emollient spray, is efficacious for the treatment of moderate psoriasis**

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**BACKGROUND:** Topical steroids are the cornerstone for the treatment of psoriasis. Most super potent corticosteroids are only indicated for 2 weeks due to their potential for atrophy and possible risk for HPA axis suppression.

**OBJECTIVE:** A novel formulation of 0.05% betamethasone dipropionate in an emollient spray vehicle (DFD-01) was developed to penetrate to the skin layers most affected by psoriasis, with a VCA equivalent to a medium potency steroid. In one study, DFD-01 showed similar efficacy in psoriasis to a super potent augmented betamethasone dipropionate 0.05% lotion. Here, we compared the efficacy and safety of DFD-01 to its vehicle for the treatment of moderate plaque psoriasis.

**METHODS:** Two Phase 3 trials randomized adults with moderate psoriasis (Investigator Global Assessment [IGA]=3; 10 to 20% BSA) 2:1 to DFD-01 or Vehicle. Products were applied twice daily to all affected areas for 28 days. Assessments included IGA, total sign score (TSS) of target lesion, local cutaneous signs and symptoms, and adverse events. Treatment success was defined as an IGA=0 or 1 and ≥2 grade improvement from baseline. Primary endpoint was the proportion of subjects achieving treatment success at day 15. Secondary endpoints included treatment success at day 29 and day 8, and the proportion of subjects with ≥50% reduction in TSS (TSS50) at day 4. Treatment success was analyzed using Cochran-Mantel-Haenszel.

**RESULTS:** Moderate psoriasis subjects were enrolled in Study 1 (174 DFD-01; 87 Vehicle) and Study 2 (182 DFD-01; 95 Vehicle). Mean BSA was between 13% and 14% for all groups. Target lesion location ranges were: elbows (24.1% to 27.0%); knees (10.3% to 14.9%); trunk (13.7% to 21.8%); and extremities (34.5% to 43.2%). Treatment success was achieved in significantly more subjects using DFD-01 compared with Vehicle at day 15 in both Study 1 (P < .001) and Study 2 (P = .002), and at day 29 (both studies P < .001). Treatment success with DFD-01 was significant at day 8 in Study 1 (P = .003) but not in Study 2 (P = .156). Day 4 TSS50 reductions were achieved in 12.1% DFD-01 vs 2.3% Vehicle in Study 1 and 14.3% DFD-01 vs 10.5% Vehicle in Study 2. TEAEs and local cutaneous signs and symptoms were similar between groups. In the pooled safety analysis, DFD-01 had a lower incidence of application site pain (pain, burning and/or stinging) than Vehicle. Safety was similar between 2 and 4 weeks.

**CONCLUSION:** DFD-01 exhibits excellent efficacy and safety for the treatment of extensive psoriasis (10-20% BSA). DFD-01 achieved treatment success in significantly more subjects than Vehicle after 2 and 4 weeks of treatment. DFD-01 improved signs of erythema, scaling and elevation in target lesions, with many located in difficult to treat areas. Both DFD-01 and its Vehicle were well tolerated with no increase in AEs between 2 and 4 weeks.

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**DISCLOSURES:** L Stein Gold reports grants and personal fees from Leo, outside the submitted work. M Jackson received grants from Promius outside the submitted work. MLF Knuckles reports personal fees and non-financial support from Abbott/Abbvie, personal fees and non-financial support from Celgene, personal fees and non-financial support from Johnsen & Johnson, personal fees and non-financial support from Amgen, personal fees and non-financial support from Galdema, personal fees and non-financial support from Taro Pharma, personal fees and non-financial support from Novartis, personal fees from Ranbaxy, personal fees and non-financial support from Novartis, personal fees from Bayer, personal fees from Sun Pharmaceuticals, other from Intraderm, outside the submitted work. JS Weiss reports grants from Promius, during the conduct of the study; personal fees from Promius, outside the submitted work.

**FUNDING:** Promius Pharma, Princeton, New Jersey.

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**PA-14: DFD-01, a novel medium potency betamethasone dipropionate 0.05% emollient spray, demonstrates similar efficacy to augmented betamethasone dipropionate 0.05% lotion for the treatment of moderate psoriasis**

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BACKGROUND: Topical steroids are commonly used for the treatment of mild-to-moderate psoriasis. Betamethasone dipropionate is available in various formulations for the treatment of corticosteroid responsive dermatoses. A novel 0.05% betamethasone dipropionate emollient spray (DFD-01) formulation has been designed to treat the layers of the skin most affected by psoriasis, maximizing efficacy and improving patient compliance.

OBJECTIVE: We compare the efficacy and safety of the medium potency DFD-01 with a super potent augmented betamethasone dipropionate 0.05% steroid lotion (Diprolene [AugBD]) for the topical treatment of moderate psoriasis.

METHODS: Adults with moderate plaque psoriasis (Investigator Global Assessment [IGA]=3; 10 to 20% BSA) were randomized 2:1:1 to receive DFD-01, AugBD, or Vehicle Spray. Products were applied twice daily to all affected areas on the body excluding face, scalp, and intertriginous areas for 14 days. IGA was assessed at baseline, day 8 and day 15. Treatment success was defined as an IGA=0 or 1 and ≥2 grade improvement from baseline. Total sign scores (TSS) for a target lesion (the sum of erythema, plaque and elevation scores) were assessed at baseline, day 4, day 8 and day 15. Local cutaneous safety and treatment-emergent adverse events (TEAEs) were recorded. Treatment success was analyzed using Cochran-Mantel-Haenszel.

RESULTS: 351 subjects with moderate psoriasis were randomized to DFD-01 (n=174), AugBD (n=90), or Vehicle (n=87). Mean baseline BSA was 13% to 14% across groups. Treatment success was achieved in 19.0% DFD-01, 18.9% AugBD, and 2.3% Vehicle (P < .001 DFD-01 vs Vehicle) at day 15. Treatment success at day 8 was 10% DFD-01, 6.7% AugBD, and 1.2% Vehicle (P = .003 DFD-01 vs Vehicle). TSS of target lesions steadily reduced over time in both the DFD-01 (day 4: -17.3%; day 8: -31.4%; day 15: -43.4%) and AugBD groups (day 4: -10.6%; day 8: -27.8%; day 15: -37.4%), while Vehicle TSS appeared to level out after an initial decline (day 4: -10.5%; day 8: -20.7%; day 15: -16.7%). Local cutaneous signs and symptoms were similar between DFD-01 and AugBD with the exception of more burning/stinging reported with AugBD than DFD 01 (13.6% vs 4.1%, P = .006). No differences were seen in the incidence of TEAEs between groups at day 15. The majority of AEs were mild, with application site AEs the most frequently reported. Lower levels of pain (pain, burning and/or stinging) at the treatment site was reported for DFD-01 compared with AugBD (14.4% vs 7.5%, P = .084) while application site pruritus was similar.

CONCLUSION: Medium potency DFD-01 was efficacious for the treatment of moderate psoriasis. DFD-01 demonstrated similar efficacy to the super potent AugBD steroid lotion. Results at 4 and 8 days indicate that DFD-01 shows early improvement in some patients. DFD-01 was well-tolerated and had an excellent safety profile.

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DISCLOSURES: J Fowler reports grants from Promius, during the conduct of the study. AA Hebert reports The University of Texas received funds to conduct the research protocol. J Sugarman reports no disclosures.

FUNDING: Promius Pharma, Princeton, New Jersey.

PA-15: Dose-finding clinical study with ingenol mebutate for field treatment of actinic keratosis up to 250 cm² on full face, scalp, or chest

Hanke CW, 1 Berman B, 2 Swanson N, 3 Pariser DM, 4 Weiss J, 5 Bukhalo M, 6 Skov T, 7 Villumsen J, 7 Siegel D 8


BACKGROUND: Ingenol mebutate (IngMeb) is approved for the field treatment of actinic keratosis (AK) in areas up to 25 cm². OBJECTIVE: This Phase 1/2 clinical study investigated the efficacy and safety of IngMeb in larger areas on the face, scalp, and chest. Here, we report the Phase 2 part of the trial. The doses studied in Phase 2 were selected in the dose-escalation part of the study.

METHODS: Randomized, double-blind, parallel-group, vehicle-controlled, 8-week, clinical study (NCT01820260) investigating efficacy and safety of 0.018% (0.018) and 0.027% (0.027) IngMeb gel for larger areas applied as field treatment once daily for 2 or 3 consecutive days (2D or 3D) to the full face, balding scalp (25-250 cm²), or approximately 250 cm² on the chest, in patients with 5-20 clinically typical AKs in the treatment area. Six components of local skin responses (LSRs)—erythema, flaking/scaling, crusting/swelling, pustulation/vesiculation, and erosion/ulceration—were scored 0-4, yielding a maximum composite LSR score of 24. Efficacy was assessed by AK count on days 29 and 56; LSRs and adverse events were assessed on days 1, 3/4, 8, 15, 29, and 56. Patients completed a burning sensation diary on all treatment days, and a Treatment Satisfaction Questionnaire for Medication on day 56.

RESULTS: 313 patients were randomized and received active treatment or vehicle. In each treatment group, at least 92% of patients completed all treatments. Median age was 67 years, 79% were men, all were white, 94% had Fitzpatrick skin type I-III, and the median history of AK was 10 years. The baseline mean AK count range was 9.4-11.9 across treatment groups.
Complete clearance at week 8 was achieved by 21%-39% of patients treated with IngMeb, a significantly greater proportion than with vehicle (0%-3%; P < .02). At week 8, reduction in AK count from baseline was significantly greater with IngMeb than vehicle: 70.5% (0.018, 2D); 67.7% (0.027, 2D); 73.5% (0.018, 3D); and 82.9% (0.027, 3D) vs 15.7% (2D); 4.3% (3D) P < .001, with a dose response trend, and the 0.027, 3D group was significantly greater than in the other active groups (P < .02). For all active doses, the composite LSR score peaked on the day after last application (day 3/4), rapidly declined, and was near baseline at 2 weeks. The mean peak composite LSR score for the 4 active treatments showed a dose-response trend and was higher than for vehicle (range 8.0-11.0 vs 1.9, respectively). All active treatments were well tolerated, with the most common adverse drug reactions being application-site pain/burning (IngMeb, 87.5%-93.8% vs vehicle, 6.5%-12.9%) and application-site pruritus (14.1%-29.0% vs 0%). Burning intensity was predominantly mild or moderate. There were no treatment-related serious adverse events. Global treatment satisfaction was high for all active treatments and significantly higher than for vehicle (75.9%-81.4% vs 28.6%-37.6%; P < .001).

LIMITATIONS: Phase 2 trial with limited amount of data. A limited number of doses were evaluated.

CONCLUSION: All active treatments of IngMeb gel for larger areas were effective and well tolerated as field treatment of AK on the full face, scalp, or a large area on the chest.

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PA-16: Efficacy of ixekizumab in patients with and without previous experience with biologic therapies compared to etanercept and placebo in patients with moderate-to-severe plaque psoriasis

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BACKGROUND: Ixekizumab is an anti-IL-17A monoclonal antibody.

OBJECTIVE: This subgroup analysis evaluated the efficacy of ixekizumab compared with placebo and etanercept in patients (pts) with moderate-to-severe plaque psoriasis with or without previous experience with biologic therapy.

METHODS: 1,224 pts were randomized to receive either placebo (n = 168), or etanercept 50 mg biweekly (n = 358), or ixekizumab 80 mg subcutaneously once every 2 weeks (IXE Q2W, n = 351) or 4 weeks (IXE Q4W, n = 347) after an initial dose of 160-mg at Week 0. At Week 12, the proportions of pts with at least ≥75% improvement in Psoriasis Area and Severity Index (PASI 75), a static physician global assessment of 0 or 1 (sPGA 0,1), and a 100% improvement in PASI (PASI 100) were evaluated in subgroups of pts with previous exposure to biologics and pts naïve to biologic therapy. Treatment groups were compared using Fisher’s exact test within each subgroup and missing values were imputed as nonresponse.

RESULTS: Overall, 288 patients had received prior biologic treatment and 936 were biologic-naïve. In both subgroups, respective PASI 75 response rates with IXE Q2W (92.9% and 88.8%) and IXE Q4W (74.1% and 78.6%) were significantly greater than those with placebo (0% and 3.2%; P < .05) and etanercept (30.3% and 44.3%; P < .05). Similarly, sPGA 0.1 response rates with IXE Q2W (84.5% and 82.8%) and IXE Q4W (67.1% and 74.8%) were significantly greater than those with placebo (0% and 3.2%) and etanercept (30.3% and 37.6%). The respective proportions of patients with PASI 100 in the biologic-experienced and biologic-naïve subgroups were also significantly higher with IXE Q2W (48.8% and 37.8%) and IXE Q4W (22.4% and 33.6%) compared with placebo (0% and 0.8%, P < .05) and etanercept (5.3% and 5.3%, P < .05).

LIMITATIONS: Results are limited to the 12-week induction period of this trial. Patients with prior etanercept exposure were excluded from enrollment in this trial.

CONCLUSIONS: In this subgroup analysis, both ixekizumab dose regimens (IXE Q2W and IXE Q4W) were significantly more effective in the treatment of psoriasis than either placebo or etanercept in pts who had prior exposure to biologic therapy or who were biologic-naïve.
PA-17: Efinaconazole topical solution, 10%: efficacy in onychomycosis patients when co-existing tinea pedis is treated with luliconazole cream, 1%

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BACKGROUND: Tinea pedis leads to onychomycosis and yet there are little data looking at the treatment of both diseases.

OBJECTIVE: To evaluate efficacy of efinaconazole topical solution, 10% in onychomycosis patients when co-existing tinea pedis is treated with luliconazole cream, 1%.

METHODS: An analysis of 1655 patients, aged 18-70 years, randomized to receive efinaconazole topical solution, 10% or vehicle from two identical multicenter, double-blind, vehicle-controlled 48-week studies evaluating safety and efficacy. The primary end point was complete cure rate (0% clinical involvement of target toenail, and both negative potassium hydroxide examination and fungal culture) at week 52. Efficacy was assessed in a subpopulation of patients where co-existing tinea pedis at baseline was treated with once-daily luliconazole cream, 1%, or another physician-preferred antifungal.

RESULTS: Overall, complete cure rates for efinaconazole were 18.5% (observed case, pooled data) at week 52.1 At baseline, 340 (20.5%) patients were reported as having co-existing tinea pedis. Efinaconazole topical solution, 10% was significantly more effective than vehicle when treating onychomycosis in these patients (P < .001, all primary and secondary endpoints, week 52). Complete cure rates of 35.3% (observed case, pooled data) were reported at week 52 in those efinaconazole patients where co-existing tinea pedis was treated with luliconazole cream, 1%, compared with 25.0% when another antifungal was used.

LIMITATIONS: Treatment of onychomycosis for 48 weeks may be too short to determine treatment success in some patients.

CONCLUSION: Treatment of co-existing tinea pedis in onychomycosis patients with luliconazole cream, 1% appears to enhance the efficacy of once daily topical efinaconazole topical solution, 10%.
PA-19: Evaluation of the appearance of nail polish following daily treatment of ex vivo human fingernails with topical solutions of tavaborole or efinaconazole

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BACKGROUND: Patients with onychomycosis mask infected nails with polish. Tavaborole topical solution, 5% is a novel, boron-based, small-molecule for treatment of toenail onychomycosis caused by Trichophyton rubrum & T. mentagrophytes; efinaconazole topical solution, 10% approved for the same indication.

OBJECTIVE: Efinaconazole package insert instructs against use of nail polish during treatment. We evaluated: 1) nail polish appearance after daily dosing with tavaborole and efinaconazole applicators; 2) applicator appearance after daily dosing of solutions on polished nails; and 3) color transfer from applicators.

METHODS: Twelve ex vivo human nails were cleaned and polished with two coats of L'Oreal Nail Color, Devil Wears Red #420 nail polish. Nails were treated with tavaborole or efinaconazole solutions qd X 7 days. Dropper and brush applicators were used to apply the solutions to white watercolor paper immediately after dosing nails to assess color transfer from the polish. Nails, applicators, & watercolor papers were photographed daily.

RESULTS: Tavaborole-treated polished nails showed no signs of polish discoloration and tavaborole applicators did not change in appearance. No color transfer from polished nails was evident on the applicator or paper. Efinaconazole-treated polished nails showed polish irregularities after the first day of treatment, with polish appearance progressively worsening over 7 days of treatment. Polish color transfer from nails to applicator, paper, and solution remaining in the bottle was evident.

CONCLUSION: Daily application of tavaborole to ex vivo polished nails did not alter nail polish appearance, while application of efinaconazole substantially altered polish and polish transfer from nails to applicators. Previous studies demonstrated effective penetration of tavaborole through the nail plate in the presence of ≤4 layers of nail polish. Together, these results suggest tavaborole treatment may be compatible with use of nail polish.

PA-20: Experience in patients with a history of malignancy in the Poriasis Longitudinal Assessment and Registry Study

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BACKGROUND: Limited information exists on the risk of malignancy in pts with a history of malignancy subsequently treated with biologic agents, as such pts are typically excluded from clinical trials.

OBJECTIVE: We report the experience of pts treated with biologics in PSOLAR, stratified by prior or no history of malignancy.

METHODS: PSOLAR is an international, longitudinal, observational study evaluating long-term safety & clinical outcomes for patients eligible to receive systemic therapy for psoriasis. Patients were stratified by those who reported a history of malignancy (other than nonmelanoma skin cancer[NMSC]) at enrollment and those who did not. Malignancies are defined according to the MedDRA System Organ Class of Malignancies. Clinical characteristics and incidence rates of cancers other than NMSC in PSOLAR overall & by exposure to any biologic or non-biologic are reported through the most recent data cut-off date (Aug 23, 2013).

RESULTS: Current data in PSOLAR reflect 12095 patients, and a median duration of follow-up of 2.5 years. Total pt-years of follow-up was 31,818; and among those with and without a history of malignancy was 1,451 and 30,366. Baseline demographics among pts with a history of malignancy were: mean(SD) age 60.0 yrs (12.2), 59.0% female, mean (SD) BMI 30.7kg/m2 (6.8), current/prior history of smoking 62.9%; among patients...
with no history of malignancy: mean (SD) age 48.1 yrs (13.8),
55.6% male, mean (SD) BMI 30.9kg/m² (7.2), current/prior history
of smoking 56.3%. Biologic exposure on registry included ustekinumab, infliximab, adalimumab, and etanercept; non-
biologic therapy on registry included methotrexate and cyclo-
sporine and phototherapy. Cumulative incidence rates per 100
pt-years among patients with a history of malignancy (exclud-
ing NMSc) were: patient exposed to biologics during registry
2.50 (95% CI:1.62,3.69), patients exposed to nonbiologic ther-
apy 3.78 (95% CI: 2.20, 6.05), all registry population2.89 (95%
CI:2.09,3.91); corresponding rates among pts with no his-
tory of malignancy were: 0.57 (95% CI:0.48, 0.68), 0.55 (95%
CI:0.36,0.79), and 0.57 (95% CI: 0.49, 0.66).
LIMITATIONS: Data have not been adjusted for differences
among subgroups (eg, age & smoking history), other malignan-
cy risk factors, and subgroups are variable in size.
CONCLUSION: In PSOLAR, pts with a history of malignancy
(other than skin cancer) had higher rates of malignancy in fol-
low-up than those patients who did not. Taking into account
limitations, the preliminary experience suggests rates are com-
parable in pts treated with biologics vs those who were treated
with alternate therapies, whether or not there was a history of
malignancy. As data accrue, future analyses may better assess
the relationship between particular biologics & malignancy.
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PA-21: Fixed combination aerosol foam formulation of
calcipotriene plus betamethasone dipropionate is well
tolerated in patients with psoriasis vulgaris: pooled data
from three randomized controlled studies

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BACKGROUND: An innovative alcohol-free aerosol foam for-
mulation of fixed-combination calcipotriene 0.005% (Cal) plus
betamethasone dipropionate 0.064% (BD) has demonstrated
superior efficacy compared with Cal/BD ointment and each of
the individual active ingredients. It is important to establish that
this superior efficacy is not associated with an increased fre-
quency or severity of adverse events (AEs). Pooling safety data
from multiple studies increases the number of exposed pa-
tients, thereby improving the precision of safety assessments
and increasing the sensitivity to rare events.
OBJECTIVE: This pooled analysis of three Phase II/III clinical
studies assessed the safety/tolerability of Cal/BD aerosol foam
over 4 weeks.
METHODS: Patients (aged ≥18 years) had mild-to-severe psoriasis
(based on physician’s global assessment of disease severity),
involving 2%-30% body surface area, with a modified
(excluding the head) psoriasis area and severity index (mPASI)
score ≥2. All three pooled studies were 4-week, randomized,
multicenter and blinded, and evaluated Cal/BD aerosol foam
versus different comparators: Cal aerosol foam, BD aerosol
foam (NCT01536938); Cal/BD ointment, aerosol foam ve-
hicle, ointment vehicle (NCT01536886); aerosol foam vehicle
NCT01866163). All AEs reported across the three studies were
re-coded according to the Medical Dictionary for Regulatory
Activities version 15.1. Adverse drug reactions (ADRs) were
AEs for which the investigator had not described the causal
relationship to trial medication as ‘not related’.
RESULTS: Overall, 1,104 patients were randomized across
the three studies to Cal/BD aerosol foam (n = 564), Cal aerosol
foam (n = 101), BD aerosol foam (n = 101), aerosol foam vehicle
(n = 152), Cal/BD ointment (n = 135) or ointment vehicle (n =
51). All patients were included in the safety analysis set. 1,050
patients (95.1%) completed 4 weeks, including 543 (96.3%)
receiving Cal/BD aerosol foam; only two patients (0.4%) with-
drew from Cal/BD aerosol foam as a result of AEs. 95 AEs were
reported in 78 patients (13.8%) receiving Cal/BD aerosol foam;
similar event rates were observed in the other active treatment
groups. The most common AEs with Cal/BD aerosol foam were
nasopharyngitis (n=6, 1.1%) and application-site pain (n = 4,
0.7%); most AEs were mild (n = 71/95; 74.7%). Three serious
AEs were reported in three patients receiving Cal/BD aerosol
foam (hypersensitivity, bipolar disorder, substance-induced
psychotic disorder), with only the hypersensitivity considered
possibly treatment related. ADRs experienced by ≥2 patients
receiving Cal/BD aerosol foam were application-site pain (n
3; 0.5%) and application-site pruritus (n = 2, 0.4%). No le-
sional/perilesional AE was reported in ≥1% of patients receiv-
ing Cal/BD aerosol foam. There were no clinically relevant
changes in albumin-corrected serum calcium and spot urinary
calcium:creatinine ratio during Cal/BD aerosol foam treatment.
LIMITATIONS: Cal/BD aerosol foam was only evaluated over a
4-week period, thus not allowing for the evaluation of AEs
potentially associated with longer-term use.
CONCLUSION: This 4-week pooled analysis in a large patient
population demonstrates a positive benefit–risk profile for Cal/
BD aerosol foam; the superior efficacy shown compared to Cal/
BD ointment and the individual active ingredients is not associ-
ated with poorer tolerability.
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PA-22: Ixekizumab impact on itch severity compared to etanercept and placebo: results from UNCOVER-2, a phase 3 trial in patients with moderate-to-severe plaque psoriasis

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BACKGROUND: Itch is a significant and persistent symptom affecting many psoriasis patients and is associated with markedly decreased quality of life.

OBJECTIVE: To evaluate the effect of ixekizumab treatment on itching severity in patients with psoriasis compared to etanercept and placebo.

METHODS: In this trial, 1,224 patients with psoriasis were randomized to receive subcutaneous placebo (n = 168), etanercept (50 mg twice weekly; n = 358), or a single 80 mg injection of ixekizumab once every 2 (IXE Q2W; n = 351) or 4 weeks (IXE Q4W; n = 347) following a 160-mg initial dose at Week 0. Itching severity was assessed using the Itch Numeric Rating Scale (Itch NRS), a patient-reported, single-item, 11-point scale where 0 represents “no itch” and 10 represents “worst itch imaginable” in the past 24 hours. Improvement in itch and the percentage of patients with a prespecified response (≥4-point score reduction from baseline) or with Itch NRS=0 at Week 12 were compared between treatment groups using mixed effects model for continuous variables and the Fisher exact test or a logistic model for categorical variables after imputing the missing values using nonresponder imputation (NRI).

RESULTS: Average baseline Itch NRS score across groups was 48.3 and 47.6, respectively. Greater improvements in DLQI scores of 0 or 1 indicate no impact of skin disease on HRQoL. The SF-36 Physical (PCS) and Mental (MCS) component summary scores are derived from the eight SF-36 domains (scored 0-100). The proportion of patients who achieved a DLQI score of 0 or 1 at Week 12 and changes in DLQI total score, PCS, and MCS scores from baseline to Week 12 were compared between treatment groups.

RESULTS: The average baseline DLQI score across groups was 12.3 and the average baseline SF-36 MCS and PCS were 48.3 and 47.6, respectively. Greater improvements in DLQI scores of 0 or 1 indicate no impact of skin disease on HRQoL. The SF-36 Physical (PCS) and Mental (MCS) component summary scores are derived from the eight SF-36 domains (scored 0-100). The proportion of patients who achieved a DLQI score of 0 or 1 at Week 12 and changes in DLQI total score, PCS, and MCS scores from baseline to Week 12 were compared between treatment groups.

CONCLUSIONS: Ixekizumab-treated patients reported significantly greater and more rapid improvements in itching severity as measured by the Itch NRS compared to placebo and etanercept over 12 weeks.

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FUNDING: Sponsored by Eli Lilly and Company.

PA-23: Ixekizumab impact on health-related quality of life compared to etanercept and placebo: results from UNCOVER-2, a phase 3 trial in patients with moderate-to-severe plaque psoriasis

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BACKGROUND: Psoriasis has a significant impact on health-related quality of life (HRQoL).

OBJECTIVE: To understand the impact on HRQoL after 12 weeks of treatment with ixekizumab, an anti-IL-17A monoclonal antibody, compared to etanercept or placebo.

METHODS: In this trial, 1,224 patients were randomized to receive subcutaneous placebo (n = 168), etanercept (50 mg twice weekly; n = 358), or a single injection of 80 mg ixekizumab every 2 weeks (IXE Q2W; n = 351) or every 4 weeks (IXE Q4W; n = 347) following a 160-mg starting dose at Week 0. HRQoL was assessed with the Dermatology Life Quality Index (DLQI) and the SF-36. DLQI scores of 0 or 1 indicate no impact of skin disease on HRQoL. The SF-36 Physical (PCS) and Mental (MCS) component summary scores are derived from the eight SF-36 domains (scored 0-100). The proportion of patients who achieved a DLQI score of 0 or 1 at Week 12 and changes in DLQI total score, PCS, and MCS scores from baseline to Week 12 were compared between treatment groups.

RESULTS: The average baseline Itch NRS score across groups was 6.6. Significant improvements in itching severity were observed compared to placebo and etanercept (P < .001) as early as Week 1. By Week 12, changes in Itch NRS scores in the IXE Q2W (-5.2) and IXE Q4W (-4.9) treatment groups remained significantly larger compared to placebo (-0.4; P < .001) and etanercept (-3.6; P < .001). Among patients with baseline Itch NRS of ≥4 points, the proportions of patients who had a ≥4-point reduction in Itch NRS scores were significantly greater in the IXE Q2W (84.8%) and IXE Q4W (76.8%) groups versus placebo (14.1%; P < .001) and etanercept (57.2%; P < .001). More patients had Itch NRS=0 at Week 12 in the IXE Q2W (40.7%) and IXE Q4W (40.6%) groups compared to placebo (2.4%; P < .001) and etanercept (17.3%; P < .001).

LIMITATIONS: Results are limited to the 12 week induction period of this trial.

CONCLUSIONS: Ixekizumab-treated patients reported significantly greater and more rapid improvements in itching severity as measured by the Itch NRS compared to placebo and etanercept over 12 weeks.

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FUNDING: Sponsored by Eli Lilly and Company.
were observed as early as first postbaseline assessment at Week 2 for the ixekizumab treatment groups compared to placebo and etanercept (P < .05). At Week 12, more patients in the IXE Q2W (64%) and IXE Q4W (60%) groups had a DLQI score of 0 or 1 versus placebo (6%; P < .05) or etanercept (34%; P < .05). At Week 12, greater improvements in the SF-36 PCS were observed in the IXE Q2W (3.8) and IXE Q4W (4.6) groups versus placebo (-0.5; P < .05) and etanercept (2.6; P < .05). There were greater improvements in the SF-36 MCS in the IXE Q2W (4.5) and IXE Q4W (2.9) groups versus placebo (-0.1; P < .05) and in the IXE Q2W group versus etanercept (2.4; P < .05).

LIMITATIONS: Results are limited to the 12 week induction period of this trial.

CONCLUSION: Ixekizumab-treated patients reported significantly greater and more rapid improvements in HRQoL as measured by DLQI or SF-36 compared to placebo and etanercept over 12 weeks, and more than 60% patients reported no impact of psoriasis on HRQoL with a DLQI score of 0 or 1.

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PA-24: Maintenance of efficacy results from UNCOVER-1: a phase 3 trial of ixekizumab for moderate-to-severe plaque psoriasis

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**BACKGROUND:** IL-17A plays a key role in the pathogenesis of psoriasis.

**OBJECTIVE:** The objective of this study was to evaluate the safety and optimal dosing interval for ixekizumab, an anti–IL-17A monoclonal antibody, in the maintenance of response during an additional 48 weeks of blinded treatment among patients who achieved an sPGA 0/1 following 12 weeks of induction therapy.

**METHODS:** In this trial, 1,296 patients were randomized to receive subcutaneous placebo (n = 431), or a single injection of 80 mg ixekizumab every 2 (IXE Q2W; n = 433) or 4 weeks (IXE Q4W; n = 432 following a 160-mg starting dose at Week 0. At Week 12, ixekizumab-treated patients who achieved sPGA 0/1 were re-randomized to receive placebo (n = 226), 80 mg ixekizumab every 4 (IXE Q4W; n = 229) or 12 weeks (IXE Q12W; n = 227). Patients in any treatment arm, who did not achieve sPGA 0/1 at Week 12, received IXE Q4W through Week 60. Comparisons were done using logistic regression analysis. For response analyses, missing data was imputed using nonre-
sponder imputation method.

**RESULTS:** At Week 60, sPGA 0/1 was maintained in 72.9%, 37.4%, and 7.5% of patients in the IXE Q4W, Q12W, and placebo groups, respectively (P < .001 for each comparison vs placebo). Complete resolution of psoriasis (PASI 100) was achieved at Week 60 by 52.0%, 20.3%, and 2.7% of patients in the IXE Q4W, Q12W, and placebo groups, respectively (P < .001 for each comparison vs placebo). Exposure-adjusted, serious adverse event (SAE) rates (per 100 person-years) in the re-randomized population were 8.0, 5.8, and 6.8 in the IXE Q4W, Q12W, and placebo groups, respectively. By comparison, SAE rates at Week 12 were 6.0, 12.2, and 5.2, for IXE Q2W, Q4W, and placebo groups, respectively.

**LIMITATIONS:** A limitation of the trial was the lack of an active comparator group.

**CONCLUSION:** IXE Q4W was effective at maintaining sPGA 0/1 over 60 weeks and over 50% of patients achieved complete resolution of their psoriasis by Week 60. These results provide further evidence for the long-term effectiveness of ixekizumab. The exposure-adjusted SAE rates in patients re-randomized to the Q4W dose were comparable in the maintenance period through Week 60 relative to the 12-week induction period.

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PA-25: Psoriasis patients with PASI 90 response achieve greater HRQOL improvements than those with PASI 75-89

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BACKGROUND: Secukinumab was evaluated in two phase 3 studies in subjects with moderate-to-severe plaque psoriasis. OBJECTIVE: This analysis evaluates the benefit of secukinumab on patient-reported outcome (PRO) responses of achieving improvements in objective skin clearing (as defined by PASI 90 status vs. PASI 75-89 status).

METHODS: Patients aged ≥ 18 years were randomized 1:1:1 in ERASURE to secukinumab 150mg, secukinumab 300mg, and placebo and 1:1:1:1 in FIXTURE including an etanercept 50mg. PROs were assessed using the Dermatology Life Quality Index (DLQI) and the visual analog scale (VAS) from the EuroQoL 5-Dimension Health Status Questionnaire (EQ-5D) at baseline and weeks 4, 8, 12, 24, 36, and 52. Subjects achieving clinical response (PASI 90 or PASI 75-89) and PRO meaningful response (DLQI [0 or1] or EQ-5D VAS (>7 points) were compared using the chi-square test.

RESULTS: Among the 1,144 subjects randomized to secukinumab, 550 (48.3%) were PASI 90 responders, and 292 (25.5%) were PASI 75-89 responders at week 12. Subjects achieving both clinical response and DLQI response were significantly higher among the PASI 90 compared with PASI 75-89 responders at week 12 (70.0% vs 48.1%; P < .05). A numerically larger proportion of subjects achieved PASI 90 response and EQ-5D VAS response at week 12 versus PASI 75-89 (73.8% for PASI 90 vs 70.9% for PASI 75-89; P > .05).

LIMITATIONS: The analysis population comprised patients who participated in clinical trials and may not be representative of this patient population as a whole.

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

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DISCLOSURES: L. McLeod is an employee of RTI Health Solutions. T Fox is an employee of Novartis Pharma AG. Y Zhao is an employee of Novartis Pharmaceuticals Corporation. M Mordin is an employee of RTI Health Solutions. B Strober is on advisory boards for AbbVie, Amgen Inc, Celgene, Dermira, Janssen, Eli Lilly and Company, Medac, Novartis, Pfizer, UCB Pharma; is a consultant for AbbVie, Amgen Inc, Celgene, Dermira, Eli Lilly and Company, Janssen, Medac, Novartis, Pfizer, UCB Pharma Xenoport; and a paid speaker for AbbVie.
RESULTS: Overall, there have been a total of 5,433 patients who received treatment with adalimumab in clinical trials with no reported cases of demyelinating disorders. For infliximab a total of 2,503 patients were involved in investigator led studies, and only one case of demyelinating disease was reported. Finally, one case of multiple sclerosis was identified out of 7,135 patients treated with etanercept. There were 26 individual cases of demyelinating disorders from TNFi treatment reported as case series or case reports. The majority of these patients had complete resolution of neurological symptoms upon cessation of TNFi therapy with or without interventional therapy.

LIMITATIONS: While this review covered the three most commonly prescribed TNFi- etanercept, adalimumab, and infliximab-the two recent TNFi-golimumab and certolizumab pegol were not investigated.

CONCLUSION: Although there are potential immunologic bases of TNF blockade leading to demyelination of the central and peripheral nervous systems, the results of the present review suggest that demyelinating diseases associated with TNFi are rare. The majority of patients included in this study have achieved full recovery in the long-term with minimal disease relapse.

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DISCLOSURES: The authors have nothing to disclose.

PA-27: Safety of adalimumab dosed every week and every other week in patients with hidradenitis suppurativa or psoriasis

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BACKGROUND: Adalimumab (ADA) is approved for the treatment of moderate-to-severe plaque psoriasis (Ps) at a dose of 40 mg every other week (eow) and is being investigated for the treatment of hidradenitis suppurativa (HS).

OBJECTIVE: We report the safety of ADA dosing 40 mg eow and every week (ew) in these patient (pt) populations.

METHODS: n 2 phase 3, double-blind, placebo-controlled studies, pts with HS who received ADA ew in period A (12 weeks) were randomized to receive placebo (Pbo), or 40-mg ADA eow or ew in period B (24 weeks). In an open-label extension (OLE) study for phase 2/3 studies in Ps, pts received 40-mg ADA eow; from weeks 24 to 252, pts with <50% improvement in PASI could escalate the dose to 40-mg ew; afterwards, they were re-evaluated at 6 and 12 weeks and then every 12 weeks. Upon achieving a PASI75 response, pts who dose escalated were de-escalated to eow. Pts who de-escalated and fell below PASI50 again were re-escalated to ew and kept there. Adverse events (AEs) are presented as number of events and events per 100 pt-years (n, [E/100 PY]).

RESULTS: Overall, 300 pts with HS in period B and 1605 with Ps in the OLE were included. In patients with HS, the AE rate was lower in the ew (163 [492.4]) and ew (167 [471.8]) groups compared with Pbo (188 [591.2]). Serious AEs were reported at higher rates in the ew (7 [21.1]) and ew (5 [14.1]) groups compared with the Pbo group (2 [6.3]); however, rates of AEs leading to discontinuation were comparable. Infection rates in the ew (46 [139.0]) and ew (45 [127.1]) groups were lower compared with the Pbo group (55 [173.0]). Other AEs of interest occurred infrequently. Among pts with Ps, the rates of AEs and serious AEs were comparable between the ew and ew groups (any: ew 6623 [237.6] vs ew 517 [232.5] and serious: ew 181 [6.5] vs ew 17 [7.6]; the rate of AEs leading to discontinuation was higher with ew dosing (ew 80 [2.9] vs ew 22 [9.9]). Infection rates were lower with ew dosing (144 [64.8]) compared with ew dosing (2029 [72.8]), and rates of serious infections were comparable (ew 33 [1.2] vs ew 2 [0.9]).

CONCLUSION: Regardless of treatment assignment, the incidence of AEs appears higher in pts with HS, compared with pts with Ps, which may be due to inherent characteristics of the HS population. In pts with HS or Ps, the safety of ADA ew and eow dosing regimens was comparable and consistent with the expected AE profile of ADA.

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DISCLOSURES: CL Leonardi was paid for work by commercial organizations either directly or indirectly through an intermediary by AbbVie, Amgen, Celgene, Coherus, Dermira, Eli Lilly, Galderma, Janssen, Leo, Merck, Novartis, Pfizer, Sanofi, Stiefel, UC B, and Wyeth. CW Lynde was paid for work by commercial organizations either directly or indirectly through an intermediary by AbbVie, Amgen, Boehringer, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Novartis, and Regeneron; he received reimbursement of travelling, accommodation and hospitality expenses from commercial organizations: AbbVie, Amgen, Boehringer, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Novartis, and Regeneron. D Arikan, HD Teixeira, and M Karunaratne receive a salary as employees of AbbVie and may also receive AbbVie stock, stock options and/or stock grants. M Okun is a former employee of AbbVie and is now affiliated with Fort HealthCare.

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PA-28: Satisfaction with current psoriasis treatment: misalignment between physician and patient perceptions

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BACKGROUND: Psoriasis is a chronic, immune-mediated, skin disorder where a well-established physician patient relationship is instrumental to obtain the best successful disease outcome.

OBJECTIVE: To examine whether there is misalignment between dermatologists and their psoriasis patients regarding satisfaction with current psoriasis therapies.

METHODS: Data from the Adelphi 2011 and 2013 Psoriasis Disease Specific Programmes, surveys of US dermatologists and their patients, were pooled for this analysis. Dermatologists provided patient treatment history, while patients reported data on health-related quality of life (HRQoL) using the EuroQoL 5-Dimension Health Questionnaire (EQ-5D) and Dermatology Life Quality Index (DLQI). Work productivity loss was measured using the Work Productivity Activity index (WPAI). Physicians and patients independently reported their satisfaction with psoriasis control (satisfied, dissatisfied). Two levels of satisfaction alignment between physician and patient responses were constructed and compared: aligned (same responses) and misaligned (different responses). Multivariate regressions examined the relationship between satisfaction alignment overall disease and symptom severity, while controlling for differences in patient demographics and comorbidities.

RESULTS: From 627 paired dermatologist and psoriasis patient records, 512 (81.7%) and 115 (18.3%) cases fell into the ‘aligned’ and ‘misaligned’ groups, respectively. Compared with patients in the aligned group, those in the misaligned group had more moderate-to-severe psoriasis (82.3% vs 43.7%), psoriasis-related moderate-to-severe itching (45.6% vs 27.8%), pain (23.0% vs 10.6%), and scaling (54.8% vs 36.1%), and had lower current biologics use (27.0% vs 42%) (all \(P < .05\)). The misaligned group was associated with reduced HRQoL (lower EQ-5D score: 0.86 vs 0.91; higher DLQI score: 7.06 vs 4.23) and greater work productivity loss (higher WPAI scores: 18.27 vs 11.43) (all \(P < .05\)). Multivariate analyses confirmed these results (\(P < .05\)).

LIMITATIONS: Patients who had consulted with their dermatologist were invited to participate. As such, the patient sample may not be fully representative of the wider psoriasis patient population.

CONCLUSION: Almost 1 in 5 patients were misaligned with their dermatologist’s level of satisfaction with their psoriasis treatment; misalignment was associated with increased disease and symptom severity, and reduced HRQoL and work productivity. These findings demonstrate that there is a need for different tools to more objectively evaluate treatment performance, increase alignment and improve patient outcomes.

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PA-29: Secukinumab 300 mg shows superior efficacy across subject body weight groups: pooled analysis of phase 3 ERASURE and FIXTURE trials

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BACKGROUND: Obesity is a frequent comorbidity in plaque psoriasis. Response to biologics, including etanercept, is known to be reduced with increasing body weight. Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile.

OBJECTIVE: In this analysis, pooled responses from the Phase 3 ERASURE and FIXTURE trials were analyzed by body weight quartile.

METHODS: Secukinumab 300 mg and 150 mg was evaluated vs placebo in moderate-to-severe plaque psoriasis in ERASURE (738 subjects) and vs etanercept 50 mg and placebo in FIXTURE (1306 subjects). Secukinumab was administered at baseline, Weeks (Wk) 1, 2 and 3, then every 4 weeks from Wk 4 to 48, with follow-up to Wk 52. Co-primary endpoints were Psoriasis Area and Severity Index (PASI) 75 and Investigator’s Global Assessment 2011 modified version (IGA mod 2011 0/1) responses at Wk 12 vs placebo. Secondary endpoints included PASI 90 response at Wk 12 vs placebo. Randomization was stratified by body weight (<90 kg or ≥90 kg).

RESULTS: Subjects were grouped by baseline weight quartile: 42–69.9kg, 70–82.0kg, 82.1–97kg, and 97.1–219.1kg. PASI 75, IGA mod 2011 0/1 and PASI 90 responses (non-responder imputation) were numerically lower with increasing weight at Wk 12, Wk 16 and Wk 52. At Wk 12, PASI 75 response with 300 mg secukinumab was 82.1% in the lowest weight quartile vs 70.6% in the highest (72.1% vs 58.9% with 150 mg). All efficacy outcomes favored 300 mg over 150 mg at Wk 12, Wk 16 and Wk 52 across all weight quartiles. PASI 75 response rates were between 7.6% and 11.8% higher with secukinumab 300 mg than with 150 mg at Wk 12 and between 9.7% and 18.0% higher with 300 mg at Wk 52. PASI 90 response rates were between 6.2% and 24.9% higher with secukinumab 300 mg than with 150 mg at Wk 12 and between 12.9% and 27.8% higher with 300 mg at Wk 52. No new or unexpected safety signals were observed.

CONCLUSION: Secukinumab 300 mg demonstrated consistently greater benefit than the 150 mg dose across weight quartiles, even in the highest where responses trended slightly lower. In all subgroups, substantial and durable PASI 75 and PASI 90 responses were achieved.

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Background: Interleukin (IL)-17A is a key proinflammatory cytokine in the pathogenesis of plaque psoriasis. Secukinumab, a fully human monoclonal antibody (mAb) that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile. In general, mAbs are immunogenic to varying extents, which can lead to hypersensitivity reactions and/or compromise therapeutic efficacy. In vitro assays are commonly used to assess immunogenicity. Secukinumab exhibits low immunogenicity in clinical trials and human in vitro assays.

Objective: The objective of the study was to investigate secukinumab immunogenicity, its effects on the action of secukinumab, and potential molecular and mechanistic explanations of immunogenicity.

Methods: Secukinumab immunogenicity was evaluated in blood samples from subjects with moderate-to-severe plaque psoriasis at baseline and at weeks 12, 24, and 52 in 6 phase 3 studies. Samples were tested with a highly sensitive assay established and validated in accordance with current guidelines. Treatment-emergent anti-drug antibodies (TE-ADA) were defined as a positive ADA signal detected in post-treatment samples (any time point) from subjects with a negative baseline signal. Confirmed TE-ADA samples were further analyzed for neutralizing activity. Potential immunogenicity of secukinumab was also evaluated by applying 2 in vitro assays: MHC-associated peptide proteomics (MAPPS) and a T-cell assay. For the MAPPS assay, monocyte-derived dendritic cells (DC) from healthy subjects were exposed to different marketed biotherapeutic proteins as well as secukinumab. DCs naturally process proteins and present HLA class II–associated peptides that can be derived from various regions of a protein sequence. The number of presented sequence regions in a protein, as well as the frequency with which they occur in the cohort of subjects, correlates with immunogenic potential.

Results: The number of presented sequence regions obtained from 15 healthy subject DC samples exposed to secukinumab was low and comparable to biotherapeutics known to exhibit low clinical immunogenicity. TE-ADA were detected in 0.4% of subjects receiving any secukinumab dose. Development of TE-ADA or neutralizing antibodies was not associated with loss of efficacy or other issues of clinical concern. The T-cell assay quantified responses to protein therapeutics in samples from 50 healthy, drug naïve subjects with a broad range of HLA class II haplotypes. The percentage of donors responding to secukinumab in the T-cell assay was low (6%) and comparable to biologics of known low immunogenicity.

Conclusion: Results from in vitro MAPPS and T-cell assays are consistent with the clinically observed low immunogenicity rate in secukinumab treated subjects with plaque psoriasis.

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PA-31: Secukinumab efficacy in anti-TNF-naïve and anti-TNF-IR patients with psoriatic arthritis: results of a phase 3 multicenter, double-blind, placebo-controlled study (FUTURE 2)

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BACKGROUND: Secukinumab, a human anti-IL-17A monoclonal antibody, demonstrated significant efficacy in the randomized, double-blind, placebo-controlled phase 3 FUTURE 2 study (NCT01752634).

OBJECTIVE: The current analyses evaluate secukinumab efficacy by prior tumor necrosis factor inhibitor (anti-TNF) therapy status.

METHODS: 397 adults with active psoriatic arthritis (PsA) were randomized to subcutaneous secukinumab (300, 150 or 75 mg) or placebo at baseline, Week (Wk) 1, 2, 3, 4 and every 4 weeks thereafter. Patients were stratified according to inadequate response or intolerance to prior anti-TNF therapy (anti-TNF-IR), or no prior exposure (anti-TNF-naïve). The primary endpoint was American College of Rheumatology 20 (ACR20) response at Wk 24. Secondary endpoints were Psoriasis Area and Severity Index (PASI) 75/90 response, Disease Activity Score 28 using C-reactive protein (DAS28-CRP), Short Form-36 Physical Component Summary (SF-36 PCS), Health Assessment Questionnaire-Disability Index (HAQ-DI), ACR50, dactylitis and enthesitis.

RESULTS: 35% of patients enrolled were anti-TNF-IR and 65% were anti-TNF-naïve. At Wk 24, ACR20 responses were greater with secukinumab vs placebo regardless of anti-TNF status. The highest responses were generally observed among anti-TNF-naïve patients. Improvements were observed with secukinumab vs placebo for secondary endpoints of ACR50, PASI 75/90, DAS28-CRP, dactylitis, enthesitis, SF-36 PCS and HAQ-DI in both anti-TNF-IR and anti-TNF-naïve patients. Greatest improvements in the anti-TNF-IR group were generally observed with secukinumab 300 mg.

CONCLUSION: Efficacy was demonstrated with secukinumab 300 mg and 150 mg in both anti-TNF-naïve and anti-TNF-IR patients, with secukinumab 300 mg being associated with the highest responses in anti-TNF-IR patients.

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PA-32: Secukinumab impact on psoriasis experiences: analysis of psoriasis symptom diary from ERASURE and FIXTURE

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BACKGROUND: Secukinumab, a fully human anti-interleukin 17A monoclonal antibody, was evaluated in ERASURE and FIXTURE, two phase 3 multicenter double blind vs placebo clinical studies for efficacy and safety in subjects with moderate-to-severe plaque psoriasis. Treatment effect was assessed using clinical measures such as the Psoriasis Area and Severity Index (PASI) and the ‘new’ Psoriasis Symptom Diary (PSD), which measures both the severity and bothersomeness of psoriasis-related symptoms.

OBJECTIVE: The objective of this study was to measure treatment effect as assessed by PASI and PSD.

METHODS: Patients aged ≥ 18 years were randomized 1:1:1 in ERASURE to receive subcutaneous treatment with secukinumab 300 mg, secukinumab 150 mg, or placebo; and 1:1:1:1 in FIXTURE which included etanercept 50 mg twice-weekly. Patients were asked to evaluate their psoriasis symptoms and experiences over the previous 24 hours. Weekly scores were derived as averages of daily 0-to-10 numerical ratings (higher scores indicative of greater severity/bothersomeness). Analyses focused on itching, pain and scaling. Absolute change from baseline to week 12 for the weekly average was analyzed using ANCOVA with covariates: geographical region, body weight stratum, and baseline value. Differences between treatment groups were determined using LS means and 95% CI. Among patients on secukinumab, differences in the bothersomeness of psoriasis-related symptoms between patients achieving clinical response (i.e. PASI 90 or PASI 75) and those not achieving clinical response (not reaching PASI 75) at week 12 were also examined.

RESULTS: Approximately 40% of patients completed the voluntary PSD. For the pooled analysis, subjects treated with secukinumab had significantly greater reductions in the bothersomeness of psoriasis-related itching, pain, and scaling than those treated with placebo or etanercept (all, P < 0.01). Patients treated with secukinumab (ERASURE n = 187, FIXTURE n = 266) who achieved PASI 90 clinical response had greater reductions in PSD itching and scaling bothersomeness than those who achieved PASI 75, and both achieved greater relief than patients who did not achieve clinical response (all P < 0.05).

LIMITATION: A limitation of this study was that the PSD was voluntary and completed by approximately 40% of subjects. Evaluations of the clinical and demographic characteristics of the sample provide evidence that subjects who completed the PSD are similar to the overall trial population.

CONCLUSION: Secukinumab offered significantly greater relief of the bothersomeness of psoriasis-related itching, pain, and scaling compared to placebo or etanercept. Greater skin clearance as assessed by PASI (PASI 90 vs. PASI 75) was related to greater relief in the bothersomeness of patient-reported, psoriasis-related symptoms.

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PA-33: Secukinumab in psoriasis: relationship between clinical and PRO using data from th ERASURE AND FIXTURE trials

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BACKGROUND: Secukinumab, a fully human anti-interleukin 17A monoclonal antibody, was evaluated in ERASURE and FIXTURE, two phase 3 multicenter double blind vs placebo clinical studies, for efficacy and safety in subjects with moderate-to-severe plaque psoriasis.

OBJECTIVE: Data from these trials provided an opportunity to
evaluate the relationship between traditional clinical outcomes and patient-reported symptoms.

**METHODS:** Patients aged ≥ 18 years were randomized 1:1:1 in ERASURE to receive subcutaneous treatment with secukinumab 300 mg, secukinumab 150 mg, or placebo; and 1:1:1:1 in FIXTURE which included etanercept 50 mg twice-weekly. The co-primary endpoints were the Psoriasis Area and Severity Index (PASI) and Investigator’s Global Assessment Mod 2011 Rating Scale (IGA mod 2011). Symptom response was evaluated using the patient-completed Psoriasis Symptom Diary (PSD), which measures psoriasis-related disease characteristics which subjects have reported as important and relevant to their disease and treatment. Correlation coefficients were calculated at baseline, week 12, and from baseline to week 12 between the PSD weekly itching, pain and scaling scores and the PASI and IGA mod 2011 scores. Logistic regression evaluated the relationship between itching, pain and scaling response (improvement of at least 2.2 points for itching and pain and 2.3 points for scaling), and percent change in PASI at week 12.

**RESULTS:** Approximately 40% of patients completed the voluntary PSD. For the pooled analysis (ERASURE, n = 187; FIXTURE, n = 266) of secukinumab data, correlation coefficients at baseline were positive but low in magnitude (0.11-0.21) and positive and stronger at week 12 (0.32-0.52). The change from baseline to week 12 correlation coefficients (0.18-0.30) were positive but lower in magnitude than week 12 values. Most coefficients were significant (P < .001). The logistic models showed that the percent change in PASI score was a significant predictor of PSD response. The likelihood of a response for psoriasis-related itching, pain, and scaling at week 12 increased from 77.7%, 65.9% and 77.7% with a 75% PASI change between baseline and week 12 to 85.9%, 72.6%, and 86.1% with a 90% PASI change.

**LIMITATION:** A limitation of this study was that the PSD was voluntary and completed by approximately 40% of subjects. Evaluations of the clinical and demographic characteristics of the sample provide evidence that subjects who completed the PSD are similar to the overall trial population.

**CONCLUSION:** PASI 90 provides greater symptom response as measured by the PSD than PASI 75. It is important to evaluate both patient-reported outcomes and clinical endpoints to understand the full benefits of a psoriasis treatment.

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**PA-34: Secukinumab is effective in subjects with moderate-to-severe palmoplantar psoriasis: 16-week results from the GESTURE study**

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**BACKGROUND:** Palmoplantar psoriasis, psoriasis involvement of the palms and soles, occurs in up to 40% of plaque psoriasis patients. Pain, functional limitations, a severe impact on patients’ quality of life and resistance to treatment is often associated with palmoplantar psoriasis. Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile.

**OBJECTIVE:** The purpose of this study was to evaluate the efficacy and safety of secukinumab in subjects with moderate-to-severe palmoplantar psoriasis (palmoplantar Investigator’s Global Assessment (ppIGA) ≥3).

**METHODS:** GESTURE is a double-blind, randomized, placebo-controlled, parallel-group multicenter phase 3b study. Subjects (N = 205) were randomized 1:1:1 to receive either secukinumab 300 mg, secukinumab 150 mg or placebo sub-
cutaneously; secukinumab treatment was continued until Week 132, and placebo until Week 80. At Week (Wk) 16 subjects in the placebo group who did not achieve a ppIGA 0 or 1 were re-randomized 1:1 to receive either 300 mg or 150 mg secukinumab. The primary objective was to demonstrate superiority of secukinumab 300 mg and/or 150 mg over placebo as assessed by ppIGA 0 or 1 (0=clear, 1=almost clear/minimal psoriasis of palms and soles) response at Wk 16. Data were analysed using the Cochran-Mantel-Haenszel (CMH) test with Non-Responder Imputation (NRI) and a sensitivity analysis using Multiple Imputations (MI). Secondary objectives included the evaluation of palmoplantar Psoriasis Area and Severity Index (ppPASI) over time, as well as overall safety and tolerability.

RESULTS: The primary and secondary endpoints at Wk 16 were met. ppIGA 0 or 1 response at Wk 16 with both doses of secukinumab was superior to placebo (P < .001); NRI: 33.3%, 22.1%, 1.5%; MI: 39.4%, 23.1%, 1.5%, for secukinumab 300 mg, 150 mg and placebo, respectively. ppPASI reduction from Baseline at Wk 16 was greater compared to placebo for both doses of secukinumab (P < .001): -54.6%, -35.3%, -4.1%, for secukinumab 300 mg, 150 mg and placebo, respectively. The most common adverse events reported across all treatment arms were headache, nasopharyngitis and upper respiratory tract infection, similar to other pivotal phase 3 studies of secukinumab in psoriasis.

CONCLUSION: Results from the GESTURE study are the most robust data on palmoplantar psoriasis and show that secukinumab is efficacious with an acceptable safety profile. GESTURE is at the largest randomized, double-blind, placebo-controlled study evaluating the effects of an intervention in this difficult-to-treat psoriasis population.

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PA-35: Secukinumab is predominantly prescribed at the recommended 300 mg does to psoriasis patients in the United States

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BACKGROUND: Secukinumab is a novel, fully human monoclonal antibody indicated for the treatment of moderate-to-severe plaque psoriasis, and has been available to US patients since March of 2015. According to the US product label, the recommended dose is 300 mg. For some patients, a dose of 150 mg may be acceptable.

OBJECTIVE: To examine the profile of secukinumab patients and the dosage prescribed in the real world.

METHODS: Secukinumab Service Request Forms (SRFs) jointly filled by physicians and patients for initial secukinumab prescriptions from March 1, 2015 to May 31, 2015 were analyzed. All patients provided written informed consent. Information on the prescribed secukinumab dose and patient characteristics was analyzed descriptively.

RESULTS: The analysis included 5,050 secukinumab SRFs completed by 1,989 unique physicians. Patients were from all regions of the US: Northeast (14.5%), Midwest (20.2%), South (45.6%), and West (19.7%). The patient sample was roughly balanced by sex (females, 45.7%; males, 53.8%; missing data, 0.5%) and distributed across a wide range of age groups: 18-24 years (2.6%), 25-34 (10.6%), 35-44 (20.4%), 45-54 (25.1%), 55-64 (25.2%), 65+ (16.2%). 2,494 patients (49.4%) had previously used a biologic (missing or unknown for rest of data), with 60% (1,486) using 2 or more biologics. Overall, the initial secukinumab dose was 300 mg for 99.9% of the patients (5,046) and 150 mg for only 4 patients (0.1%). A majority of the SRFs requested the autoinjector pen as the injection device (4,543; 90.0%) rather than the pre-filled syringe (507; 10.0%).

LIMITATIONS: Only patients captured in the secukinumab SRFs were analyzed.

CONCLUSION: Using a large number of secukinumab SRFs filled by US patients and their physicians distributed from all
PA-36: Secukinumab is superior to ustekinumab in clearing the skin and leads to greater improvement in QOL of subjects with moderate-to-severe plaque psoriasis: 16-week results from the CLEAR study

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BACKGROUND: Secukinumab, a fully human monoclonal antibody (mAb) that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile. Ustekinumab is a human mAb directed against IL-12 and IL-23.

OBJECTIVE: The objective of this study was to demonstrate superiority of secukinumab to ustekinumab in achieving Psoriasis Area and Severity Index (PASI) 90 response.

METHODS: CLEAR is a phase 3b study comparing efficacy/safety of secukinumab vs ustekinumab, an anti-IL-12/23 mAb, in adults with moderate to severe plaque psoriasis. In this 52-week (Wk), multicenter, double-blind, parallel-group, active comparator-controlled study (NCT02074982), subjects were randomized 1:1 to subcutaneous injection of secukinumab (300 mg) or ustekinumab (per label, for subjects ≤100 kg, 45 mg; >100 kg, 90 mg). In both arms, randomization was stratified by body weight (≤100 and >100 kg). Secukinumab was administered at baseline, Wks 1, 2 and 3, then every 4 weeks from Wk 4 to 48; ustekinumab at baseline and Wk 4, then every 12 weeks from Wk 16 to 40. Primary objective: superiority of secukinumab vs ustekinumab in PASI 90 response at Wk 16. Secondary objective: superiority in speed of onset (PASI 75 response at Wk 4). Subjects reported on health related quality of life (QOL), including the Dermatology Life Quality Index (DLQI). PASI results reported here are based on multiple imputation, a statistical technique for handling missing efficacy data that is recognized by health authorities and increasingly used in the analysis of trial data.

RESULTS: Secukinumab (80.1%; n=334) was superior to ustekinumab (59.5%; n=335) in the proportion of PASI 90 responders at Wk 16 (P < .0001). More patients on secukinumab (45.0%) achieved PASI 100 response (clear skin) at Wk 16 than with ustekinumab (29.3%; P < .0001). Secukinumab was superior in speed of onset than ustekinumab: PASI 75 response at Wk 4 was 50.3% for secukinumab vs. 20.9% for ustekinumab (P < .0001). The percentage of subjects achieving DLQI score of 0 or 1 (indicative of no effect on QOL) was significantly higher with secukinumab (71.9%) than with ustekinumab (57.4%) at Wk 16 (P < .0001). Secukinumab’s safety profile was comparable to ustekinumab and consistent with safety data from secukinumab pivotal phase 3 studies.

CONCLUSION: Secukinumab treatment has demonstrated superiority to ustekinumab at Wk 16 in clearing skin of subjects with moderate-to-severe psoriasis and achieved a better QOL improvement, with faster onset of efficacy and a comparable safety profile.

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OBJECTIVE: To analyze the pooled safety data from two phase 3 randomized controlled trials (FUTURE 1 and FUTURE 2).

METHODS: Safety data from two randomized, double-blind, placebo-controlled, phase 3 studies in patients with active PsA, FUTURE 1 (NCT01392326) and FUTURE 2 (NCT01752634), were pooled. In FUTURE 1, 606 patients were randomized to secukinumab or placebo. Patients on secukinumab received 10 mg/kg i.v. at baseline, Week (Wk) 2, and 4, followed by 75 or 150 mg s.c. every 4 weeks from Wk 8. Placebo was given according to the same i.v. and s.c. schedule. In FUTURE 2, 397 patients were randomized to receive s.c. secukinumab (300, 150, or 75 mg) or placebo at baseline, Wk 1, 2, 3, 4, and every 4 weeks thereafter. At Wk 16, placebo patients with ≤20% reduction in both tender and swollen joint count (nonresponders) were re-randomized to receive secukinumab 75 or 150 mg s.c. in FUTURE 1 and secukinumab 300 or 150 mg s.c. in FUTURE 2; respondents were re-randomized at Wk 24. Anti-drug antibodies (ADAs) were assessed using a Meso Scale Discovery bridging assay with a stepwise approach for screening, confirmation and titration. All randomized patients were included in the pooled safety analysis.

RESULTS: 974 patients received ≥1 dose of secukinumab (955 patient-years of exposure). Baseline demographics, disease/medical history and concomitant medications were similar between the pooled secukinumab and placebo populations. During the 16-Wk placebo-controlled period, adverse events (AEs)/serious AEs (SAEs) were reported in 58.9%/3.4% and 58.3%/4.0% of patients in the pooled secukinumab and placebo groups, respectively. Exposure-adjusted AE/SAE incidence rates across the entire safety period (mean/max exposure: 358.1/721 days secukinumab; 128.6/233 days placebo) were 210.3/9.0 and 319.6/13.6 per 100 patient-years with secukinumab and placebo, respectively; 25 (2.6%) patients receiving secukinumab discontinued due to AEs during this period vs 14 (4.7%) with placebo. Nasopharyngitis and upper respiratory tract infection were the most frequent AEs with secukinumab and placebo in both the placebo-controlled period and throughout the entire safety period. There was one death due to intracranial hemorrhage in a patient with a history of CV disease who received secukinumab. The incidence of inflammatory bowel disease/ Crohn's, Candida infections, neutropenia, MACE and malignancy was low with secukinumab. Injection site reactions with secukinumab were observed in 26 (2.7%) patients vs 3 (1.0%) with placebo. Treatment-emergent ADAs were detected in 1 (0.1%) patient, with no associated loss of efficacy.

CONCLUSION: Secukinumab was well-tolerated in patients with active PsA, with a low incidence of SAEs and discontinuations due to AEs, and a low potential for immunogenicity.

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**PA-38:** Secukinumab shows efficacy in subjects regardless of previous exposure to biologic therapy: a pooled subanalysis from four phase 3 clinical trials in psoriasis

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**BACKGROUND:** Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile. **OBJECTIVE:** This analysis evaluates the effect of prior biologic exposure on responsiveness to secukinumab.

**METHODS:** ERASURE, FIXTURE, FEATURE, and JUNCTURE were randomized, double-blind, placebo-controlled, multicenter, phase 3 studies evaluating secukinumab efficacy at Week (Wk) 12 in subjects with moderate-to-severe plaque psoriasis (secukinumab 300 and 150 mg s.c. vs placebo; and vs etanercept in FIXTURE). Designs and methodology of primary studies have been reported elsewhere. In this pooled subanalysis, the effect of previous biologic exposure on response to secukinumab treatment was evaluated with respect to Psoriasis Area and Severity Index (PASI) 90 and 100 responses at Wk 12. Results for FIXTURE etanercept arm are not reported due to low subject number.

**RESULTS:** Wk 12 mean PASI 90 response rates in subjects without prior exposure to biologics and treated with secukinumab 300 mg or 150 mg vs placebo were 58.1% and 44.6% vs 1.3% (each dose \(P < .0001\) vs placebo. For each dose, risk difference comparator estimate and 95% CI were, respectively, 56.8%, 51.7 – 61.6; 43.3%, 37.8 – 48.6). In comparison, Wk 12 mean PASI 90 response rates were slightly lower in subjects with prior exposure to biologics and treated with secukinumab 300 mg or 150 mg vs placebo (50.7% and 29.4% vs 0.7%; each dose \(P < .0001\) vs placebo; 50.0%, 39.4 – 59.2; 28.7%, 17.7 – 39.1). At Wk 12, in the subset with prior biologic treatment failure, PASI 90 response rates in subjects treated with secukinumab 300 mg or 150 mg vs placebo were 42.0% and 27.5% vs 1.8% (each dose \(P < .0001\) vs placebo; 40.2%, 21.8 – 56.5; 25.8%, 8.2 – 42.1). In the subject subset with responses to prior biologic treatment, PASI 90 response rates in subjects treated with secukinumab 300 mg or 150 mg vs placebo were 55.2% and 30.8% vs 0% (each dose \(P < .0001\) vs placebo; 55.2%, 42.3 – 66.4; 30.8%, 16.0 – 44.5). Both doses (300 mg > 150 mg) in each subset resulted in significantly higher responses compared with placebo. PASI 100 response rates were similar to PASI 90 for all subgroups.

**CONCLUSION:** These data suggest secukinumab significantly improves responses vs placebo in subjects with moderate-to-severe plaque psoriasis regardless of prior exposure to biologic therapy and regardless of response to prior biologic therapy.

**DISCLOSURES:** CEM Griffiths reports grants and personal fees from Novartis, during the conduct of the study; grants and personal fees from AbbVie, grants and personal fees from Actelion, and personal fees from Bioteck, and personal fees from Celgene, and personal fees from GSK-Stiefel, and personal fees from Incyte, and grants and personal fees from Janssen, and grants and personal fees from LEO Pharma, and grants and personal fees from Merck Sharp & Dohme, and grants and personal fees from Pfizer, and grants and personal fees from Tridant, and grants and personal fees from UCB, outside the submitted work. K Papp reports grants and personal fees from Novartis, during the conduct of the study; grants and personal fees from Novartis, grants and personal fees from Amgen, and personal fees from Astellas,

**PA-39:** Secukinumab significantly reduces psoriasis burden in patients with psoriatic arthritis: results from the phase 3, FUTURE 2 study

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BACKGROUND: Reducing psoriasis burden in subjects with active psoriatic arthritis (PsA) and concomitant psoriasis is an important aspect of disease management. The randomized, double-blind, placebo-controlled phase 3 FUTURE 2 study (NCT01752634) demonstrated that secukinumab, a human anti-IL-17A monoclonal antibody, significantly improved the signs and symptoms of active PsA and provided an opportunity to evaluate the impact on skin disease burden.

OBJECTIVE: The effects of subcutaneous (s.c.) secukinumab on dermatological parameters in the FUTURE 2 study are presented here.

METHODS: 397 adults with active PsA were randomized to s.c. secukinumab (300, 150 or 75 mg) or placebo at baseline, Week (Wk) 1, 2, 3, 4 and then every 4 weeks thereafter. The primary endpoint was American College of Rheumatology 20 (ACR20) response at Wk 24. Assessments of psoriasis burden included ≥75% and ≥90% improvement in Psoriasis Area and Severity Index (PASI) 75/90. The primary endpoint and PASI 75/90 secondary endpoints were included in a hierarchical testing analysis and were adjusted for multiplicity at Wk 24. Other assessments were exploratory endpoints. Exploratory skin assessments were Investigator's Global Assessment (modified 2011) score of 0 or 1 (IGA 0/1), and the Dermatology Life Quality Index (DLQI). All skin assessments were undertaken in patients with psoriasis affecting ≥3% of body surface area. Effect of treatment on modified Nail Psoriasis Severity Index (mNAPSI) was assessed in patients with nail involvement. The effect of treatment on the inflammatory marker high-sensitivity C-reactive protein (hsCRP) was monitored in all patients.

RESULTS: At Wk 24, PASI 75/90 response rates were significantly improved with secukinumab 300 and 150 mg vs placebo. Secukinumab also improved IGA 0/1 and mNAPSI scores, reduced hsCRP levels and provided clinically meaningful improvement (≥4-point change from baseline) in DLQI vs placebo at Wk 24.

CONCLUSION: Secukinumab 300 and 150 mg s.c. reduced the severity of plaque and nail psoriasis and improved skin-related quality of life in subjects with active PsA and significant concomitant psoriasis burden.

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PA-40: Secukinumab treatment maintains efficacy in moderate-to-severe plaque psoriasis through second year of treatment: a randomized extension of the ERASURE and FIXTURE studies

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BACKGROUND: Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early...
time points, with a sustained effect and favorable safety profile. This trial is a 4-year extension of two 1-year secukinumab phase 3 studies in moderate-to-severe psoriasis (ERASURE, FIXTURE).

OBJECTIVE: This abstract focuses on results at Week (Wk) 104 in subjects who were Psoriasis Area and Severity Index (PASI) 75 responders at the end of the core studies (Wk 52).

METHODS: PASI 75 responders from the trials’ secukinumab treatment arms were randomized 2:1 to continue the same doses of secukinumab (300 mg or 150 mg, treatment arm) or receive placebo (300 mg-placebo or 150 mg-placebo, treatment withdrawal arm) every 4 weeks up to Wk 104, or until relapse (defined as a loss of >50% of the maximum PASI gain compared to the baseline of the core studies). Subjects were retreated with secukinumab 300 mg or 150 mg following relapse while on 300 mg-placebo or 150 mg-placebo, respectively. PASI 75/90/100 responses over time were assessed. Multiple imputation was used for missing data. The safety/tolerability of secukinumab up to Wk 104 was also evaluated.

RESULTS: Secukinumab 300 mg was consistently more efficacious than 150 mg, with strong sustained efficacy to Wk 104. A majority of subjects in the 300 mg (87.1%) and 150 mg (72.8%) continuous-treatment arms reached Wk 104 without experiencing a relapse, vs 16.0% and 12.7%, respectively, in the 300 mg-placebo and 150 mg-placebo treatment-withdrawal arms. In the 300 mg-placebo treatment-withdrawal arm, 70.3% of subjects achieved PASI 90 twelve weeks after retreatment following relapse. No new safety findings were identified.

CONCLUSION: Secukinumab 300 mg demonstrated strong and sustained efficacy over 2 years, with no new/unexpected safety findings.

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PA-41: Secukinumab treatment shows no evidence for reactivation of previous or latent TB infection in subjects with psoriasis: a pooled phase 3 safety analysis

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BACKGROUND: Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, is highly efficacious in the treatment of moderate-to-severe psoriasis, starting at early time points, with a sustained effect and favorable safety profile. Anti-TNF treatments have been associated with reactivation of latent tuberculosis infection (LTBI). Anti–IL-17A treatments do not impair TB control after 4 weeks in mice, but experience in humans is limited.

OBJECTIVE: Secukinumab safety was examined in subjects with LTBI or previously treated TB who participated in the Phase 3 secukinumab trials in plaque psoriasis: ERASURE, FIXTURE, SCULPTURE, FEATURE and JUNCTURE.

METHODS: Secukinumab 300 mg and 150 mg doses were compared to placebo in moderate-to-severe plaque psoriasis in ERASURE (738 subjects), FEATURE (177 subjects, prefilled syringe administration), and JUNCTURE (182 subjects, autoinjector administration), and compared to etanercept and placebo in FIXTURE (1306 patients). SCULPTURE assessed maintenance of response in subjects who were on either a fixed dose regimen or retreatment as needed. A Quantiferon® TB-Gold In-Tube assay was performed at screening. If LTBI was identified (defined as positive, indeterminate/positive, or indeterminate/indeterminate results of up to two tests), subjects received TB treatment according to local guidelines. Subjects with active TB were excluded from all studies.

RESULTS: Secukinumab 300 mg or 150 mg was received by 132 subjects who had either a history of TB (25) or LTBI at screening (107). Median duration of secukinumab treatment in this pooled cohort was 364 days. There were no cases of reactivation of TB in any subjects during treatment with secukinumab. LTBI was detected post-screening in four subjects (three within one week of randomization), two of whom received concomitant secukinumab and TB treatment. Of these, one subject in ERASURE who was negative for TB at baseline was diag-
nosed with LTBI following retest according to local guidelines on day 141 while on secukinumab 150mg and was then treated with isoniazid 300 mg daily. The subject completed the study without secukinumab dose interruption.

CONCLUSION: This analysis found no evidence for an association between secukinumab treatment and reactivation of TB in subjects with previously treated TB, and no evidence of active TB infection in subjects treated for LTBI following screening.

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PA-42: The aerosol foam formulation of fixed combination calcipotriene plus betamethasone dipropionate is efficacious in patients with psoriasis vulgaris: pooled data from three randomized controlled studies

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BACKGROUND: An innovative alcohol-free aerosol foam formulation of calcipotriene 0.005% (Cal)/betamethasone dipropionate 0.064% (BD) was developed as a new treatment option for patients with psoriasis. Phase II/III studies have shown that the aerosol foam formulation is efficacious for the treatment of psoriasis vulgaris.

OBJECTIVE: Data from three Phase II/III studies were pooled to increase the precision in the estimate of the effect size and to evaluate the efficacy of Cal/BD aerosol foam for 4 weeks in patients with psoriasis.

METHODS: The three pooled studies enrolled patients aged ≥18 years with mild–severe psoriasis of the body (NCT01536886, NCT01536938, NCT01866163); each study evaluated Cal/BD aerosol foam versus different comparators. All analyses were descriptive. Primary endpoint: proportion of patients clear/almost clear with ≥2-step improvement in disease severity at week 4 (according to physician’s global assessment; defined as treatment success). Additional endpoints: proportion of patients with treatment success at week 1; modified (excluding head) psoriasis area and severity index (mPASI) at weeks 1 and 4. Tertiary endpoints: proportion of patients with ≥75% reduction in mPASI (PASI75) at week 4; change in itch (according to visual analog scale [VAS]) at weeks 1 and 4. Missing values were imputed by last-observation-carried-forward, except for itch.

RESULTS: Overall, 1104 patients were randomized across the three studies to Cal/BD aerosol foam (n=564), Cal aerosol foam (n=101), BD aerosol foam (n=101), aerosol foam vehicle (n=152), Cal/BD ointment (n=135) or ointment vehicle (n=51). All patients were included in the full efficacy analysis set (intent-to-treat population). Overall completion rate was 95%. At week 4, 51% of patients using Cal/BD aerosol foam achieved treatment success, a higher proportion than all other treatment groups (Cal/BD ointment, 43%; BD aerosol foam, 31%; Cal aerosol foam, 15%; aerosol foam vehicle, 5%; ointment vehicle, 8%); treatment success rate was also superior for Cal/BD aerosol foam at week 1. Greater percentage mean decreases in mPASI with Cal/BD aerosol foam were noted versus all other treatments at week 1 (Cal/BD aerosol foam, 39%; Cal/BD ointment, 31%; BD aerosol foam, 32%; Cal aerosol foam, 27%; aerosol foam vehicle, 22%; ointment vehicle, 27%) as well as week 4 (71%, 63%, 53%, 43%, 32% and 33%, respectively). Week 4 PASI75 rates were also greater (51%, 41%, 34%, 18%, 7% and 10%, respectively). Cal/BD aerosol foam was efficacious irrespective of baseline disease severity (treatment success: 30% mild; 59% moderate; 33% severe baseline disease) and on all body areas assessed (ie arms, legs and trunk). Cal/BD aerosol foam treatment resulted in substantial alleviation of itch at week 1 (change in itch VAS: −30); itch relief further increased at week 4 (change in itch VAS: −41).

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PA-43: Time to response in patients with moderate-to-severe hidradenitis suppurativa who were treated with adalimumab: results from PIONEER I and PIONEER II

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BACKGROUND: Adalimumab (ADA) has demonstrated efficacy in as little as 2 weeks in patients with moderate-to-severe hidradenitis suppurativa (HS) in 2 phase 3 randomized, double-blind, placebo-controlled trials (PIONEER I and PIONEER II). However, time to response, an important factor in determining patient satisfaction and adherence to treatment, has not been reported.

OBJECTIVE: This post hoc analysis evaluated time to response for ADA compared with placebo in these patients.

METHODS: Adults with at least a 1-year history of moderate-to-severe HS were enrolled in the 2 studies. For the first 12 weeks of each study, patients were randomized (1:1) to receive ADA (160 mg at week 0, 80 mg at week 2, and 40 mg weekly starting at week 4) or placebo. A post hoc analysis was performed on integrated data from the 2 trials to investigate the effects of ADA or placebo on the median time to achieve HS clinical response (HiSCR), defined as ≥50% reduction in total abscess and inflammatory nodule (AN) count with no increase in abscess or draining fistula counts relative to baseline; the median time to achieve AN count reductions of ≥25%, 50%, 75%, and 100%; and the median time to disease flare (predefined as ≥25% increase in AN counts with a minimum increase of 2 relative to baseline). Time to each response was calculated using the Kaplan-Meier method; patients were censored at date of study discontinuation or last efficacy measurement. Treatment difference was analyzed using a stratified log-rank test ($\alpha = .05$), with patients stratified by study, baseline Hurley stage, and antibiotic use.

RESULTS: Combined analysis included 633 patients (ADA, n = 316; placebo, n = 317); 596 patients completed the first 12 weeks of the study (ADA, n = 300; placebo, n = 296). Data were missing for 4 patients in the placebo group. The ADA group demonstrated a significantly shorter median time to HiSCR than did the placebo group (31 days [range, 29–57] vs 92 days [range, 87–not reached]; HR, 2.437; 95% CI, 1.959, 3.031; $P < .001$). The ADA group also demonstrated shorter median time to achieve AN count reductions of ≥25% (16 vs 32 days), 50% (29 vs 86 days), and 75% (87 vs 119 days) compared with the placebo group, respectively (each $P < .001$). A 100% reduction in AN count was achieved by 25.3% and 12.8% of ADA and placebo patients, respectively, (HR, 2.120; 95% CI, 1.449–3.100; $P < .001$); median time to 100% reduction of AN count could not be calculated. Fewer patients in the ADA group experienced flares compared with the placebo group during the 12-week period (12.3% vs 35.8%; HR, 0.283; 95% CI, 0.196–0.410; $P < .001$); median time to flare could not be calculated.

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PA-44: Tofacitinib exposure-response characteristics in patients with moderate-to-severe plaque psoriasis

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BACKGROUND: Tofacitinib is an oral Janus kinase inhibitor that is being investigated for psoriasis.

OBJECTIVE: To evaluate the longitudinal relationship between tofacitinib exposure and clinical response.

METHODS: Data for this analysis were pooled from a Phase 2b (NCT00678210) and four Phase 3 studies (NCT01276639, NCT01309737, NCT01241591, NCT01186744). A non linear, longitudinal exposure-response model for Psoriasis Area and Severity Index (PASI) improvement was used to describe dose- and time-dependent changes. Selected patient characteristics were evaluated as predictors of response.

RESULTS: The analysis included 3431 patients with 17221 observations. Average systemic blood levels (Cavg) did not improve predictions relative to dose. For a typical patient (male; body weight, 86 kg; baseline PASI, 20; biologic agent naïve), 49% and 61% of patients receiving tofacitinib 5 and 10 mg BID, respectively, were predicted to achieve ≥75% improvement from baseline in PASI score at Week 16; this corresponded to ~65% and 81% of the maximum effect (Emax) on the dose response curve. Covariate evaluation suggested that heavier patients required a higher dose to achieve a similar response to lighter patients; a doubling of body weight (eg, from 60 to 120 kg) increased the dose needed to achieve 50% of Emax (ED50) 1.8-fold (90% CI 1.45, 2.20). This relationship could not be attributed to differences in pharmacokinetics (Cavg) with weight. ED50 was lower for patients who were female, biologic agent naïve or had higher baseline PASI; higher baseline PASI also resulted in slower onset of effect. Higher body weight and prior.
biologic use substantially reduced absolute clinical response. Dose response was evident in the above subpopulations; 10 mg BID consistently provided clinically meaningfully higher response vs 5 mg BID.

LIMITATIONS: Only a small number of patients had weight <60 kg or >120 kg, leading to higher uncertainty in the model predictions for these subpopulations.

CONCLUSION: While significant improvements were observed with both tofacitinib doses, dose-response characterisation in patients with psoriasis showed that tofacitinib response was reduced with higher body weight and prior biologic experience, as seen with other psoriasis therapies. Tofacitinib 10 mg BID provided clinically meaningful benefit over 5 mg BID in all subpopulations.

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DISCLOSURES: P Gupta, K Ito, H Tan, R Wolk, C Mebus, S Rottinghaus, H Valdez and S Krishnaswami are employees and shareholders of Pfizer Inc. M Hutmacher has acted as a consultant for Pfizer Inc, including conducting the analyses and interpretation of the data. K Papp has received grant/research support, has acted as a consultant and has participated in speakers’ bureaus for Pfizer Inc. L Mallbris was an employee of Pfizer Inc at the time of the analysis.

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PA-45: Treatment patterns and healthcare resource utilization (HCRU) among psoriasis patients

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BACKGROUND: Despite American Academy of Dermatology guidelines for psoriasis, studies report 37-39% of patients receive no treatment; those receiving treatment often receive topical therapy alone.

OBJECTIVE: To validate previous findings using a large, national healthcare-claims database, and provide an update on current treatment patterns.

METHODS: Psoriasis patients were ≥18 years with ≥2 outpatient or 1 inpatient visit for psoriasis (ICD-9: 696.1 or 696.0) in Truven Marketscan® claims database (2009-2011), continuously enrolled ≥6 months before and ≥12 months after first psoriasis diagnosis (index; Day 0). A control cohort without psoriasis diagnoses, matched 1:1 on age, gender, and geography, was identified. Psoriasis treatment patterns were categorized as: initial treatment (Days 0-30); and Days 31-90; 91-180; and 181-365. Combination therapies were defined hierarchically as biologics, conventional systemic (CS) without biologic, or phototherapy and/or topical (PT) without biologic or CS.

All-cause and psoriasis-associated HCRU and costs were calculated one-year post-index and compared between psoriasis patients and controls, and between initially treated and initially untreated psoriasis patients. Costs were adjusted using linear modeling.

RESULTS: Of 96,750 psoriasis patients, 39% were initially treated (89% monotherapy). Amongst those patients initially treated with monotherapy, 75% of treatment was topical, 10% CS, 8% biologic, and 7% phototherapy. Combination therapy regimens were biologic (31%), CS without biologic (37%), or PT without biologic or CS (32%). Of initially untreated psoriasis patients, 74% were untreated 180–360 days post-index. Psoriasis patients had higher rates of comorbidities, and outpatient and prescription resource use in the 6 months pre-index than controls (P < .0001). Psoriasis patients initially untreated had lower psoriasis-related prescription costs ($2,831 lower; P < .0001), and higher psoriasis-related inpatient costs ($784 higher; P < .0001) during the year post-index compared to patients initially treated. All-cause total costs were $3,723 higher for psoriasis patients compared to controls (P < .0001).

LIMITATIONS: This retrospective cohort study used a claims database; as such, only filled prescriptions were captured. In addition, clinical measures of psoriasis severity were unavailable.

CONCLUSION: Our study confirmed previous findings that psoriasis is associated with significant burden of illness relative to non-psoriasis patients. Over 60% of psoriasis patients are initially untreated, and the majority remains untreated through one year.

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PA-46: Utility of adjuvant intralesional kenalog in treatment-resistant nephrogenic systemic fibrosis

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BACKGROUND: Nephrogenic systemic fibrosis (NSF, formerly nephrogenic fibrosing dermopathy) is a systemic fibrosing disorder most commonly identified in patients with renal failure or severe renal impairment and exposure to Gadolinium containing contrast dye. First described in 2000 by Cowper et al., NSF presents with skin thickening and tethering to underlying structures, as well as “cobblestoning” and peau d’orange skin appearance.
Skin involvement is the most significant manifestation of disease, most often presenting with indurated plaques sometimes associated with alopecia, overlying epidermal atrophy, as well as significant pain. Contractures and functional limitation commonly develop with involvement of peri-articular soft tissue. There is no well-established treatment for NSF although evidence exists in case reports and small series for the use of the tyrosine kinase inhibitor imatinib. Our patient presented nearly 10 years after his gadolinium exposure. After diagnosis, he was started on imatinib with improvement in modified Rodnan scores from 34 to 18. However, there remained indurated fibrotic, painful plaques on his hands limiting his ability to work and play. We sought adjuvant therapy to improve his quality of life.

**OBJECTIVE:** The purpose of the study is to explore adjuvant treatment options for recalcitrant, symptomatic fibrotic plaques of NSF in a patient on systemic therapy.

**METHODS:** This is a single center, single patient case study. After diagnosis, the patient was started on imatinib 400mg daily. Skin thickness was measured using the modified Rodnan scoring system at initial and sequential follow up visits. Intralosional kenalog (ILK) was injected directly into plaques on bilateral palmar surfaces twice at 8 week intervals. Radial, median and ulnar nerve blocks were performed using 15mL of 1% lidocaine. A total of 6mL ILK 40mg/mL was injected into the plaques on the patient’s right hand and 8mL ILK 40mg/mL into the patient’s left hand.

**RESULTS:** There are several notable findings in this case: NSF can present many years after gadolinium exposure. Imatinib is an effective therapy to improve overall skin thickness however this improvement is slow and thicker, more indurated plaques may be recalcitrant. Significant improvement was noted in texture and thickness of the injected plaques as well as improvement in pain and flexion of both hands. This improvement has been sustained for 3 months.

**LIMITATIONS:** This is a single patient, single center study.

**CONCLUSION:** ILK can be considered for adjuvant therapy of recalcitrant, symptomatic plaques of NSF.

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