

Psoriasis and Other Papulosquamous Disorders

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Immune responses to pneumococcal vaccine of adults with chronic plaque psoriasis treated with alefacept

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RATIONALE AND GOAL: Alefacept is a fully human fusion protein that is T-lymphocyte-directed, with the ability to inhibit T-cell activation and to induce T-cell apoptosis. This mechanism of action could, in principle, affect the ability of patients receiving alefacept to mount an immune response to vaccines. This open-label, phase IV multicenter study was undertaken to assess the ability of patients with chronic plaque psoriasis (CPP) receiving alefacept to mount an immunological response to a pneumococcal vaccine.

PATIENTS AND METHODS: Patients (≥ 18 years old) with CPP involving $>5\%$ body surface area were treated with a standard 12-week course of alefacept (15 mg intramuscularly once a week). At Week 6, patients were administered a 23-valent polysaccharide pneumococcal vaccine. Anti-pneumococcal antibodies were measured at Weeks 0 (baseline), 6 (pre-challenge), 9, 12 and 33 (post-challenge). The primary endpoint was the percentage and number of patients who demonstrated a ≥ 2 -fold increase from Week 6 to Week 12 in antibody titer for ≥ 2 of the 5 pneumococcal antigens associated with more invasive disease and treatment-resistant disease (9V, 14, 18C, 19F and 23F). In addition, efficacy for treating CPP was determined using the Physician's Global Assessment (PGA) scale at Week 14. Adverse events (AE), vital signs and clinical laboratory analyses were performed at all visits.

RESULTS: Of the 43 patients enrolled, 40 completed Week 14, and 32 completed Week 33. At Week 12, doubling of antibody titers against ≥ 2 of the 5 primary pneumococcal antigens was observed in 36 patients with 24 patients demonstrating quadrupling of titers compared with Week 6. At Week 33, 25 patients had 2-fold increases in antibody levels and 15 had 4-fold increases compared with Week 6. At baseline, 38 of 42 patients had moderate or worse CPP based on PGA. After alefacept treatment, only 14 patients remained in this group; 28 patients improved to mild-to-moderate or better with 3 patients achieving almost clear status. AE were observed in 21 patients and were similar to those seen in previous studies (e.g. decreased CD4+ T-lymphocyte count, headache, nausea, etc), with the majority being mild or moderate in intensity. No serious AE were reported.

CONCLUSIONS: Alefacept was well tolerated. The safety and efficacy of alefacept was similar to published results. In adult patients with CPP treated with alefacept, 85.7% were successfully able to mount an immune response to pneumococcal vaccine.

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Two-step dosing of subcutaneous ustekinumab by body weight provides similar efficacy in heavier and lighter weight patients with moderate-to-severe psoriasis

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Background: Although fixed-dose biologics offer convenient dosing, efficacy may be affected by weight since serum drug concentrations are inversely associated with weight. Heavier patients who use fixed-dose biologics generally have lower drug concentrations leading to reduced response rates. **Objectives:** To evaluate the impact of weight on ustekinumab (UST) efficacy and to determine whether weight should be considered in dose selection.

Methods: PHOENIX 1 and PHOENIX 2 were Phase 3 clinical trials that evaluated the efficacy and safety of UST in patients with moderate-to-severe plaque psoriasis ($\geq 10\%$ of total body surface area and PASI score ≥ 12) who were candidates for phototherapy or systemic therapy. Patients were randomized to receive SC UST 45mg or 90mg at wks 0 and 4 and then q12wks or placebo with crossover to UST at wk12. To examine the impact of weight on clinical response, prespecified analyses of efficacy were conducted by weight categories in 10-kg increments (eg, 51-60 kg, 61-70 kg, etc) after steady-state drug levels were achieved (Wk28).

Results: Across both studies, 664 patients were randomized to the UST 45mg group and 667 to the UST 90mg group. Mean baseline body weights were 93.9kg and 91.0kg in PHOENIX 1 and 2, respectively. Based on the analysis by weight categories in 10-kg increments, a clear difference was evident in both studies at 100kg, such that for the subpopulation of patients over 100kg, PASI 75 response was about 20 percentage points higher in the 90 mg than in 45 mg (PASI75 response rates were 74.2% [155/209] and 54.6% [107/196] for the 90mg and 45mg groups, respectively). In patients ≤ 100 kg, response rates were similar between the groups (PASI 75 response rates were 80.8% [350/433] and 76.9% [347/451] for the 90mg and 45mg groups, respectively). These efficacy findings were paralleled by median serum UST concentrations. The median UST serum concentrations in patients weighing >100 kg who received a 90mg dose were similar to those in patients weighing ≤ 100 kg who received a 45mg dose. Patient weight did not have an impact on the safety of UST (54.7% versus 54.5% of patients had ≥ 1 adverse event in the ≤ 100 kg and >100 kg weight subgroups, respectively).

Conclusion: Two-step dosing of UST (45mg for patients weighing ≤ 100 kg and 90mg for those weighing >100 kg) provides comparable efficacy and pharmacokinetic exposure in both heavier and lighter weight patients. This two-step dosing approach optimizes efficacy and dosing convenience while minimizing serum drug exposure.

Commercial Support: Study sponsored by Centocor

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Correspondence between etanercept treatment patterns and dosing recommendations for psoriasis patients

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BACKGROUND: Etanercept is a TNF blocker indicated for treatment of moderate to severe plaque psoriasis (PsO) and psoriatic arthritis (PsA). US prescribing recommendations for PsO are 100mg/wk for 12 weeks, then 50mg/wk thereafter; recommended PsA dosing is 50mg/wk.

OBJECTIVE: To estimate the percentage of etanercept dispensed relative to prescribing recommendations for PsO and PsA patients in a large commercially-insured US population.

METHODS: A cohort of 1,795 adult patients initiated etanercept between May 1, 2004 and Sept 30, 2006, for PsO or PsA; had no rheumatoid arthritis or ankylosing spondylitis diagnosis within 360 days pre- or post-index; received no other TNF blocker or other biologic therapy within 360 days pre-index; and were enrolled for 360 days pre- and post-index. Etanercept claims with zero or negative reimbursed amounts or with extreme quantity values were excluded. Quantity was confirmed based on paid amount and days supply reported on pharmacy claims, refill interval, and expected ranges of doses per week. We report patient characteristics, concomitant treatments, initial etanercept dose, therapy persistence, percentage and timing of step-down therapy, and dosing relative to recommendations.

RESULTS: Analyzable dosing data was available for 79% of patients; 947 PsO only, 161 PsA only, and 318 PsO/PsA. Mean age was 45.4 years (SD = 10.5); 45% were female. Initial dose was 100mg/wk for 73% of PsO, 41% of PsO/PsA, and 6% of PsA patients. On average, the 687 PsO patients who initiated at 100mg/wk used the amount of drug that would be expected (101% of the expected dose) whereas PsO patients who initiated at 50mg (26%) used 73% of the expected dose based on the Prescribing Information. The majority (93%) of PsA only patients initiated at 50mg/wk, and overall used 93% of the expected dose. PsO/PsA patients did not fall clearly into PsO or PsA dosing. Approximately two thirds started at 50 mg (PsA dosing). Overall, PsO/PsA patients received 107% of the recommended PsA dose but only 82% of the PsO dose. Overall, the patients with psoriatic disease received between 92 and 98% of the expected dose depending on how PsO/PsA patients were categorized.

CONCLUSIONS: Overall, patients with psoriatic disease receive the amount of etanercept that would be expected based on the labeled dosing recommendations. It is not clear whether patients with both diagnoses are being treated primarily for skin or joint symptoms based on the dosing regimens being used.

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Topical formulation of pythione zinc in the treatment of psoriasis

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Background: Psoriasis is a chronic common condition of the skin that is still resistant to many therapies.

Aim: The efficacy of topical formulation of pythione zinc in an emollient base compared with emollient base alone in the treatment of psoriasis.

Methods: This was a randomized double blind clinical trial. Patients with psoriasis involved less than 10% of body skin areas were enrolled in the study. They were randomly allocated to one of two treatment groups. Group A was treated with topical emollient cream containing 0.25% pythione zinc and group B was treated with topical emollient cream alone twice daily for 3 months. Response to treatment was assessed with decreasing the PASI score was determined using the formula according severity of thickness, redness and scaling.

Results: Of 60 participants 30 patients in group A and 30 patients in group B completed the study. The mean of PASI score before and after treatment were 3.4 ± 1.8 and 0.9 ± 1.3 in group A ($p < 0.01$), and 4.3 ± 2 , and 3.9 ± 1.3 in group B ($p > 0.05$), and there was significant difference between the mean of PASI score at the end of the study between two groups ($p < 0.01$). The mean of the differences of the PASI score before and after treatment were 2.4 ± 2 and 0.4 ± 0.1 in A and B group respectively ($p < 0.01$). The percent of decrease in mean of PASI score were 70.5% in group A and 9.3% in group B. Five patients in group A and no patient in group B were cleared at the end of the study.

Conclusion: Topical formulation of pythione zinc in an emollient base can be used as a treatment for psoriasis.

Key words: Psoriasis, Pythione zinc, Emollient .

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A case of tuberculosis in a patient on efalizumab and etanercept for treatment of refractory palmopustular psoriasis and psoriatic arthritis

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We present a patient with a history of a positive tuberculin skin test, who presented with severe, recalcitrant palmoplantar pustular psoriasis with psoriatic arthritis whose symptoms did not resolve with monotherapy of etanercept or efalizumab alone, but did respond to a combination of both biologics. However, our patient was later found to have re-activation tuberculosis after long-term treatment. This case highlights many key points for treatment of psoriasis and psoriatic arthritis with biologics. Namely, that recalcitrant psoriatic skin lesions may have good clearing on one biologic, such as efalizumab, and arthritic symptoms can be well-controlled with etanercept, leading patients to be on two different biologics concurrently to control symptoms. However, it also highlights the importance of determining a patient's tuberculosis status and initiating adequate anti-tuberculosis therapy prior to starting treatment with etanercept.

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Enrollment update from observe-5, a long-term safety surveillance registry of etanercept therapy for psoriasis

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Background: Etanercept is a soluble tumor necrosis factor (TNF) receptor-Fc fusion protein that is FDA-approved for the treatment of moderate to severe plaque psoriasis in adults. Safety data for up to 2.5 years of continuous and interrupted treatment with etanercept for psoriasis have been reported.

OBSERVE-5 is a phase 4, prospective, multicenter, 5-year observational registry designed to collect and assess safety data from the real-world use of etanercept in the treatment of psoriasis as part of an FDA post-marketing commitment.

Methods: The study population includes patients with plaque psoriasis for whom etanercept is indicated, per prescribing information. Patients are prescribed etanercept in the course of standard medical care, based on the investigator's independent medical judgment. Once enrolled, patients initiate (or re-initiate) etanercept therapy at baseline in accordance with their prescription. Interim visits are scheduled at the investigator's discretion, but must occur at least twice yearly, or every 6 months. Patients will be followed for up to 5 years, and are allowed to discontinue etanercept therapy at any time following receipt of the baseline dose. Baseline demographics, disease characteristics, and serious adverse events, including serious infections, will be reported.

Results: As of 28 March 2008, 2510 patients have been enrolled and 2491 patients have received at least 1 dose of etanercept. Forty-eight percent (1183) of the patients were female, 82% (2038) were white/Caucasian, and the mean age (SD) was 46.3 (13.6) years. The mean (SD) disease duration at baseline was 15.7 (12.8) years and mean (SD) body surface area affected by psoriasis was 21.4% (19.9). Concomitant therapies included systemic therapy (11.1%), phototherapy (4.2%), and topical therapy (49.3%). Among patients who received at least one dose of etanercept, 143 (5.7%) discontinued from the study (62 men, 81 women). The most common reasons for discontinuation included withdrawal of consent (46, 1.8%), lost to follow-up (32, 1.3%), and ineligibility (25, 1.0%).

Conclusion: The patient enrollment goal as determined in the FDA commitment was met within the specified timeframe. Accumulating data from the ongoing OBSERVE-5 registry, representing outcomes from real-world dermatology practices, will complement the safety data from randomized, controlled trials of etanercept in patients with moderate to severe plaque psoriasis.

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Sequential therapy with cyclosporine and adalimumab in patients with severe plaque psoriasis: A series of five cases

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Background: Cyclosporine, a calcineurin inhibitor of T cells, is an effective treatment option for severe plaque psoriasis. However its duration of use is limited to one to two years due to its risk of organ toxicity while its discontinuation raises concern for relapse. Dermatologists are often reluctant to initiate cyclosporine due to the absence of a safe long term agent to transition patients to after treatment with cyclosporine. Adalimumab, a tumor necrosis factor inhibitor recently approved for the treatment of psoriasis, may provide a safe option for transition. An experience of using sequential therapy to help prevent relapse in patients transitioning from cyclosporine to adalimumab is described.

Methods: A series of five representative patients are presented. Patients were informed of the off-label nature of concomitant use of cyclosporine and adalimumab for the treatment of psoriasis.

Results: Five patients with severe generalized psoriasis ages 17, 20, 21, 31, and 41 transitioned from therapy with cyclosporine alone to adalimumab alone with a transition period of 12, 12, 11, 6 and 8 weeks respectively. During the transition period cyclosporine was individually tapered and adalimumab was self administered at a dose of 40 mg every other week. There was no significant change in Psoriasis Area Severity Index scores from the time of initiating the transition phase to 12 weeks after initiation. One patient experienced a mild return of psoriasis on the face which was treated successfully with topical 0.1% triamcinolone acetate ointment. Serum labs and blood pressure readings remained normal for all five patients during the transition period and no adverse events were noted.

Conclusion: Patients may be transitioned from cyclosporine to adalimumab through sequential therapy to minimize risk of recurrence of psoriasis. The short duration of concomitant therapy of twelve weeks or less in young healthy individuals may minimize the risk of additive immunosuppressive side effects. The safety and efficacy of sequential therapy with cyclosporine and adalimumab must be validated by larger randomized controlled studies.

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Patterns of pharmacologic care for psoriasis: Results from a large-scale, retrospective claims database

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BACKGROUND: Although the array of pharmacologic treatments for psoriasis is burgeoning, little is known about "real world" patterns of pharmacologic care for this disorder (i.e., in the absence of clinical research protocol requirements).

OBJECTIVE: To characterize patterns of pharmacologic care for psoriasis.

METHODS: Using 10 years (6/1/1997 to 7/31/2007) of Florida Medicaid administrative claims data, we identified the first documented psoriasis diagnosis ("index diagnosis") among adult (aged ≥ 18 years) enrollees. "Targeted treatments," those FDA-approved for psoriasis by 6/30/2006, were oral systemics (acitretin, cyclosporine, methotrexate) and biologics (alefacept, efalizumab, etanercept). "Treated patients" received ≥ 2 fills of the same targeted treatment within 45 days during the year following index diagnosis.

RESULTS: Among 3,137,110 adult enrollees, 7,571 (0.24%) received an index diagnosis of psoriasis. Of these, 173 (2.3%) patients received treatment; they were predominantly female (67.6%) and Caucasian (50.3%). There were 54 (31.2%) patients aged 18-39 years, 81 (46.8%) aged 40-59 years, and 38 (22.0%) aged ≥ 60 years. Among those treated, 63.6% (110/173) received oral systemics [24.3% (42/173) acitretin, 3.0% (3/173) cyclosporine, 37.6% (65/173) methotrexate], and 51.4% (89/173) biologics [0% (0/173) alefacept, 0.6% (1/173) efalizumab, 50.9% (88/173) etanercept]. Mean (SD) doses were: acitretin 26.6 (11.0) mg/day, cyclosporine 130 (61.0) mg/day (equivalent to 1.5 and 1.7 mg/kg/day for average U.S. males and females, respectively), methotrexate 17.5 (14.7) mg/week, and etanercept 67.2 (26.6) mg/week; alefacept and efalizumab had insufficient data for analysis. Median doses were: acitretin 25 mg/day, cyclosporine 100 mg/day (equivalent to 1.1 and 1.3 mg/kg/day for average U.S. males and females, respectively), methotrexate 14.7 mg/week, and etanercept 49.7 mg/week. Eighty-one percent of patients received acitretin ≤ 25 mg/day, 67% received cyclosporine ≤ 100 mg/day, 46.1% methotrexate ≤ 15.0 mg/week, and 54.5% etanercept ≤ 50 mg/week.

CONCLUSIONS: Given the burgeoning array of pharmacologic treatments for psoriasis and the scarcity of information about actual use, methods and findings reported from our study may provide a helpful benchmark for future assessment of aspects of pharmacologic care for this autoimmune disorder.

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Severity perception, disease flare patterns, treatment use and preferences among patients with psoriasis

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Objective: To assess the distribution of perceived psoriasis (PsO) disease severity and flaring, treatments used in the management of PsO, and patient preferences for treatment with respect to maintenance and flare control.

Methods: Cross-sectional data were collected via the Psoriasis Patient Study Project from January 1 – March 31, 2008. Study participants were recruited from an Internet panel, were aged ≥ 18 yrs and self-identified as having PsO. Demographics, flare frequency, medication utilization, and treatment preferences were assessed.

Results: A total of 1,006 respondents completed the survey (58% female; mean age = 50 yrs; mean 16.5 yrs of diagnosed PsO). When asked about disease severity, 54% reported mild disease, 39% moderate, and 7% severe. Overall, 33% of all PsO patients reported their disease as continuously flaring, with a significantly higher proportion of those with severe (57%) and moderate (44%) disease experiencing continuous flares compared with mild (22%; $p < 0.05$). Severe patients reported shorter lengths of time between flares (12.7 wks) compared to moderate (23.6) and mild (52.2) patients. Patients reported use of topical treatments (39%), over-the-counter drugs (25%), biologics (16%), prescription oral medications (6%), and sun/water/phototherapy (5%). Biologic use was significantly greater in patients with severe (40%) and moderate (25%) disease compared to those with mild disease (6%; $p < 0.05$). Once treated with biologics, most patients preferred to use biologics to control flares (64%) and as maintenance therapy (60%). Fewer biologic-treated patients reported continuous flares (26%; $p < 0.05$) compared to patients using oral prescription medication (43%) or topical treatments (36%).

Conclusions: Greater disease severity may be correlated with continuous flaring and decreased length of time between flares. PsO patients reported use of a variety of therapies, including biologic agents, to prevent recurrent flares and maintain remission. Those with severe disease were more likely to be biologic-experienced. Once biologic-experienced, patients preferred biologics to control disease, with effectiveness evidenced by fewer reports of continuous flares.

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Predictors of biologic use among patients with psoriasis

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Objective: To assess the predictors of biologic use in patients with moderate to severe psoriasis (PsO).

Methods: Cross-sectional data were collected via the Psoriasis Patient Study from January 1 – March 31, 2008. Study participants were recruited from an Internet panel, were aged ≥ 18 yrs and self-identified as having PsO. Biologic use was defined as currently using a biologic for treatment of PsO and the reference group included those not currently using a biologic. Bivariate analyses were used to compare the two cohorts. Significant differences were tested using chi-square in categorical variables, and t-tests in continuous variables. Using a logistic model, backward stepwise regression was conducted. The dependent variable was biologic treatment, where current biologic treatment = 1 and non-biologic users = 0. Covariates were determined based on the results of descriptive analyses and bivariate correlations.

Results: Compared to non-biologic users, at the bivariate level, biologic users differed in some demographic respects, had greater disease severity and, greater frequency of flares. They were more likely to use a prescription topical or oral treatment and phototherapy. Biologic users had more visits to providers and were more likely to be hospitalized. They also had poorer quality of life and functional status as measured by the SF-12v2, Skindex-16, and Dermatology Life Quality Index (DLQI). Biologic users also were likely to have health insurance through Medicare or Medicaid, to have prescription coverage, and to use a prescription discount card, but also have greater out-of-pocket costs. The final regression model had 89.2% concordance. Predictors of greater likelihood of biologic use included having managed care insurance, using an oral prescription treatment, receiving prescription from a dermatologist, greater disease severity, experiencing acne, experiencing psoriatic or rheumatoid arthritis, and having poor quality of life as measured by the DLQI and Skindex-16 functioning scale. Factors which predict the less likely use of biologics included: female gender, older age, some college background, use of over-the-counter topical treatment, and poor emotional functioning as measured by the Skindex-16 emotion scale.

Conclusions: Predictors of biologic use in PsO appear to include variables consistent with more severe disease, while predictors of non-biologic use include more demographic variables. Continued investigation of the appropriate use of biologics in patients with PsO is warranted.

Commercial Support: Centocor Ortho Biotech funded study

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Patient-physician dialogue in the management of moderate to severe psoriasis

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Purpose: To characterize physician consultations with patients with moderate to severe psoriasis (PsO). To date, no research has been reported on in-office conversations between physicians and patients with psoriasis.

Methods: Discussions between patients with moderate or severe PsO and dermatologists were video-and audio-recorded during one regularly-scheduled visit. Both parties were interviewed separately post-visit to capture the intent and comprehension of each. All dialogue was transcribed, analyzed and correlated using validated sociolinguistic models.

Results: Data were collected from 24 patient visits with 12 dermatologists. Dermatologists were in practice for an average of 15 years and 9 were male. Patients had an average age of 53 years (range: 29 to 81) and the majority (63%) were male. The most common interval between appointments was 2-3 months (30%), but most appointments were less frequent; 96% of the appointments were regular follow-ups. Visits were characterized by a focus on medication management, with minimal attention to symptoms, physical exam and benchmarking of progress. Specifically: -The average appointment lasted 7:34 minutes and focused on medication management, including medication changes and side-effects, which occupied half of the visit time -Symptoms were discussed for approximately one minute of an average visit, with 1.8 symptoms being discussed on average per visit -50% of patients use hedging or minimizing language to discuss their symptoms when speaking to their physician. Post-visit, 54% of physicians and 88% of patients acknowledge that patients are negatively impacted by the disease -In 50% of visits, a reduction in plaque coverage was the measure of success; however, a physical skin exam comprised only 1% (4 seconds) of a typical visit -Body area covered and benchmarking against previous coverage was discussed in only 2 (8%) visits.

Conclusions: Linguistic analysis of in-office dialogue and post-visit interviews revealed areas for improvement in both quantity and content of discussions, especially regarding quality of life and a complete discussion of symptoms. New communication strategies may help meet the specific needs of dermatologists engaging in dialogue with PsO patients.

Commercial Support: Centocor Ortho Biotech Services, LLC

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Withdrawn

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P2312

Two cases of fatal progressive multifocal leukoencephalopathy in psoriasis patients treated with efalizumab

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Progressive multifocal leukoencephalopathy (PML) has been reported in 2 efalizumab-treated psoriasis patients (pts). PML, a rare neurological disorder occurs almost exclusively in immunocompromised individuals by reactivation of the JC polyomavirus, found latent in more than 80% of healthy adults.

The first pt, a 70-year-old white male with a 20+-year history of psoriasis and comorbidities of coronary artery disease and hyperlipidemia, had been receiving efalizumab 1 mg/kg/wk for 4 years, with concomitant aspirin, clopidogrel, and pravastatin. He presented for consultation after his family noted behavioral changes, unclear speech, and confusion. A computed tomography angiogram revealed 75% stenosis of the left internal carotid; magnetic resonance imaging (MRI) analysis of the brain identified abnormalities within the periventricular white matter, including multifocal infarcts on the left side. The initial diagnosis was acute or subacute bland or thromboembolic infarct; the pt was treated with anticoagulant therapy for stroke. His neurological condition worsened and assessment by MRI indicated enlargement of cerebral sulci and cisterns. A cerebrospinal fluid (CSF) sample was obtained and diagnosis of PML was confirmed by PCR. Repeat MRI indicated extensive expansion of white matter lesions. Two weeks later he experienced an episode of ventricular fibrillation and expired.

The second pt, a 73-year-old white female with a 40-year history of psoriasis and comorbidities of hyperlipidemia and depression, had been receiving efalizumab 1 mg/kg for 3.75 years, with concomitant simvastatin, escitalopram, and aspirin. Before efalizumab therapy the pt's psoriasis had been managed with methotrexate. She was admitted to the hospital with eye movement disorders and gait problems suggestive of a brain-stem stroke; further evaluation was consistent with brain-stem injury and she was released. The symptoms worsened requiring readmission to the hospital where multiple cranial neuropathies were noted and validated by MRI that indicated extensive abnormalities in the brain stem. The symptoms were suggestive of PML; analysis of CSF fluid indicated the presence of JC virus confirming a diagnosis of PML. With a poor condition and prognosis, the pt was discharged from the hospital for hospice care. The pt expired several days later.

To date, these are the only 2 reported cases of fatal PML in efalizumab-treated psoriasis pts among 46,000 pts treated worldwide.

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Withdrawn

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P2314

Malignancies in ustekinumab-treated psoriasis patients: Comparisons to the general United States population

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Background: Ustekinumab (UST) is a fully human monoclonal antibody directed against interleukins (IL)-12 and -23 developed for the treatment of moderate-to-severe psoriasis. Pre-clinical models suggest that IL-12 and IL-23 may have opposing effects on tumor immunity. IL-12 is thought to elicit anti-tumor immune responses, while IL-23 may be pro-inflammatory, pro-angiogenic, and impair anti-tumor immune responses. Therefore, blocking IL-12 may prove detrimental, while blocking IL-23 may prove beneficial, for malignancy risk. The effect that blocking both IL-12 and IL-23 has on malignancy risk in humans has not been established.

Objective: To assess the impact of blocking both IL-12 and IL-23 on malignancy risk, the incidence of malignancies in UST psoriasis clinical trials was compared with malignancy rates expected in the general US population.

Methods: The incidences of nonmelanoma skin cancers (NMSCs) and all other malignancies (noncutaneous malignancies) were evaluated in pts with moderate-to-severe plaque psoriasis treated in Phase 2 and Phase 3 clinical trials of UST. For noncutaneous malignancies, standardized incidence ratios (SIRs) compared observed malignancy rates in UST-treated pts to rates expected in the US population adjusting for age, sex and race based on data available in the National Institutes of Health Surveillance, Epidemiology, and End Results (SEER) database (2000-2004).

Results: A total of 2266 patients were treated with UST in Phase 2/3 studies with 1.5 years of follow-up with a total of 2251 pt-years of follow-up (P-Y). In the PBO-controlled period of Phase 2/3 psoriasis trials, the incidence of noncutaneous malignancies was 0.25 per 100 P-Y for UST-treated pts (1 pt in 406 P-Y) compared with 0.57 per 100 P-Y for PBO-treated pts (1 pt in 177 P-Y F/U). The incidence of NMSC was 0.74 per 100 P-Y for UST-treated pts (3 pts in 406 P-Y) compared with 1.13 per 100 P-Y for PBO-treated pts (2 pts in 176 P-Y). In the controlled and non-controlled portions of these trials, the incidence of noncutaneous malignancies was 0.36 per 100 P-Y for UST-treated pts (8 pts in 2249 P-Y) and included: breast, colon, head and neck, kidney, prostate, and thyroid cancers. The rate of noncutaneous malignancies reported in UST-treated pts was comparable to the rate expected in the general population (SIR = 0.68 [95% confidence interval: 0.29, 1.34]). The incidence of NMSC was 0.80 per 100 P-Y for UST-treated pts (18 pts in 2245 P-Y).

Conclusions: In Phase 2/3 clinical trials, rates of NMSC and noncutaneous malignancies were low and similar between UST- and PBO-treated psoriasis pts, and the observed rate of noncutaneous malignancies was consistent with the expected background rate in the general US population. As this analysis was limited to 1.5 years of follow-up, longer follow-up is necessary and is currently ongoing.

Commercial Support: Centocor supported study

Psoriasis and Other Papulosquamous Disorders

P2315

Comparison of hospitalization and serious infections rates among patients with moderate-to-severe psoriasis treated with ustekinumab: Comparisons to a large healthcare claims database

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Objective: Ustekinumab (UST) is a novel biologic therapy that targets interleukin (IL) 12 and 23. In two Phase 1, one Phase 2 and two Phase 3, randomized and controlled trials. UST demonstrated significantly better clinical efficacy than placebo for patients (pts) with moderate-to-severe psoriasis, while safety profiles were comparable to placebo. This analysis compares rates of any hospitalization and serious infections between psoriasis pts treated with UST and psoriasis pts from a healthcare claims database in the United States (US)

Methods: Pts in the US MarketScan database are eligible employees, early retirees, and their dependents insured by employer-sponsored commercial plan and the Medicare supplemental plan. Moderate-to-severe psoriasis pts were defined as those who had psoriasis claims (ICD-9 CM 696.x.) and had been treated with systemic antipsoriatic agents, or had PUVA procedure in both 2003 and 2004. Hospitalization rate was defined as the number of pts who had ≥ 1 hospitalization per 100 patient-years during 2004. Serious infection was defined as any infection identified in the inpatient discharge diagnoses, and analyzed by the number of events per 100-pt-years. Hospitalization and serious infection in psoriasis pts treated with UST were collected during the Phase 1, 2, and 3 trials. The expected rates of the hospitalization and serious infection rates for the general psoriasis pts were calculated using the data from the claims database adjusting the age-sex distribution based on the clinical trial data. Ninety-five percent confidence intervals were calculated assuming number of events following Poisson distribution.

Results: A total of 1183 pts with moderate-to-severe psoriasis were identified from the claims database. Among those pts, 49.5% were female, and the mean age was 54.4 yrs. During the follow-up, pts from the claims database had a hospitalization rate of 11.3, and a serious infection rate of 2.2 per 100 pt-years; female and elder pts had a higher hospitalization and serious infection rate than male and younger pts. Among 2301 psoriasis pts treated with UST with 1480 pt-years of follow-up, the observed hospitalization and serious infection rates were 4.80 (3.74-6.07), and 1.01 (0.57-1.67) per 100-pt-years of follow-up, respectively, and the expected rate adjusting for age-sex distribution for hospitalization and serious infection rates were 7.21 (5.89-8.72), and 1.49 (0.93-3.25) per 100 pt-years of follow-up, respectively.

Conclusions: Rates of hospitalization and serious infections among psoriasis pts treated with UST were consistent with the expected rates observed in the general psoriasis pt population identified from the healthcare claims database.

Commercial Support: Centocor sponsored study

Psoriasis and Other Papulosquamous Disorders

P2316

Ustekinumab reduces itch, bodily pain, and fatigue in patients with moderate-to-severe psoriasis

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Objectives: This analysis examines the impact of ustekinumab on symptoms commonly associated with moderate-to-severe psoriasis, including itch, bodily pain, and fatigue, using data from a phase 3 clinical trial.

Methods: In the PHOENIX I trial, 766 patients were randomized to ustekinumab 45mg or 90mg at weeks 0 and 4 and every 12 weeks thereafter, or placebo at weeks 0 and 4 with crossover to ustekinumab at week 12. Assessments included the Itch visual analogue scale (VAS) (0 [no itch] to 10 [severe itch]) and for pain and fatigue, the SF-36 bodily pain and vitality scales (0 to 100 [higher scores indicate greater impact of pain and fatigue on quality of life]).

Results: At baseline, the mean (SD) itch score was 6.8 (2.7), and the mean (SD) bodily pain and vitality scores were 45.5 (11.4) and 49.7 (10.0), respectively. At week 12, the average change in itch score from baseline was -4.9, -5.1, and -0.8 in the ustekinumab 45mg, 90mg and placebo group, respectively, representing a median reduction of 86% in itch in the ustekinumab-treated patients compared to a 4% reduction in placebo-treated patients ($p < 0.001$ for each ustekinumab group vs. placebo). Mean change in pain score from baseline to week 12 was 4.4, 5.8, and 0.2 in the ustekinumab 45mg, 90mg and placebo group, respectively ($p < 0.005$ for each ustekinumab group vs. placebo). Specifically, 37% of patients reported moderate or more severe bodily pain at baseline. At week 12, 17% of ustekinumab-treated patients vs. 38% of placebo-treated patients reported moderate or severe bodily pain ($p < 0.01$). Similarly, the ustekinumab-treated patients demonstrated a greater improvement in vitality score (1.5 in the ustekinumab 45mg group and 1.6 in the 90mg group) than the placebo group (-1.6) ($p < 0.005$ for each ustekinumab group vs. placebo).

Conclusion: Ustekinumab improves itch, pain and fatigue in patients with moderate-to-severe psoriasis.

Commercial Support: Centocor sponsored study

Psoriasis and Other Papulosquamous Disorders

P2317

Adalimumab plus adjunctive topical therapy (calcipotriol/betamethasone) for moderate to severe psoriasis: First efficacy and safety results of the BELIEVE study

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Objective: To determine the role of adjunctive topical therapy (calcipotriol/betamethasone [C/B]) for psoriasis patients receiving adalimumab (ADA) in the Phase IIIb, multicenter European BELIEVE study.

Methods: BELIEVE patients had moderate to severe psoriasis (defined as ≥ 2 of 3 criteria: Psoriasis Area and Severity Index [PASI] ≥ 10 , affected body surface area (BSA) $\geq 10\%$, and Dermatology Life Quality Index [DLQI] ≥ 10). Patients must have failed or had intolerance or contraindications to ≥ 2 systemic therapies (≥ 1 must have been cyclosporine, methotrexate [MTX], or oral psoralen-UVA phototherapy [PUVA]). In this 16-week (wk) RCT, patients received ADA (80 mg at Wk 0, then 40 mg every other wk), and either 1) topical vehicle or 2) topical C/B, except for face, scalp, and nails (daily for 4 wks, then prn). Efficacy assessments were at baseline, and Wks 2, 4, 8, 12, and 16; safety data were collected throughout. Primary endpoint was PASI 75 at Wk 16 (missing values via nonresponder imputation and last observation carried forward for categorical and continuous data, respectively).

Results: 730 patients (366, ADA+C/B; 364, ADA+vehicle) enrolled (69% male; mean age, 45 yrs; mean weight, 85 kg). At baseline, patients had received a variety of prior treatments (cyclosporine, 55%; MTX, 70%; PUVA, 43%; biologics, 48%) and had mean PASI of 19.5, affected BSA of 33%, and DLQI of 14. For PASI 75 response rates, ADA+C/B was not superior to ADA+vehicle at Wk 16 (64.8% vs. 70.9%, $p=0.086$). Secondary endpoints showed numerical advantage favoring monotherapy (Physician's Global Assessment "Clear/Minimal": ADA+C/B, 56.6%, vs. ADA+vehicle, 64.6%, $p=0.028$; PASI 90: ADA+C/B, 38.8%, vs. ADA+vehicle, 50.3%, $p=0.002$). Initial efficacy was greater with combination vs. monotherapy (Wk-2 PASI 75: ADA+C/B, 14.8%, vs. ADA+vehicle, 5.8%, $p<0.001$; Wk-4 PASI 75: ADA+C/B, 40.7%, vs. ADA+vehicle, 32.4%, $p=0.021$). Adverse event incidences were similar between groups and consistent with previous ADA trials. Ten serious infections (4.4/100-patient-years) occurred. Four neoplasms were reported: lentigo maligna, nonmelanoma skin cancer, malignant melanoma (at 2 months of ADA therapy; patient had received >11 years of MTX), and lymphoma (at 3 wks of ADA therapy).

Conclusions: Adalimumab+C/B was not superior to monotherapy at Wk 16. Results suggested more rapid improvement with combination therapy early (first 4 wks), with a trend favoring monotherapy later. Adalimumab+C/B was well-tolerated.

Commercial Support: The work was supported by an unrestricted grant from Abbott Laboratories and was carried out by a consultancy (complete intellectual independence). The investigators had full control over all research decisions.

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P2318

Final results of a phase IV randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of efalizumab in patients with moderate-to-severe plaque psoriasis involving the scalp

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Introduction: This Phase IV randomized, double-blind, placebo-controlled study evaluated the safety and efficacy of subcutaneous (SC) efalizumab in adults with chronic moderate-to-severe plaque psoriasis with involvement of the scalp and no previous exposure to efalizumab.

Methods: The study consisted of a screening period, a double-blind treatment period, an open-label treatment period, and an observation/follow-up period. The primary objective was to evaluate the efficacy of a 12-week course of SC efalizumab compared with placebo in adults with chronic moderate-to-severe plaque psoriasis involving the scalp, as measured by the proportion of patients achieving a $\geq 75\%$ decrease of Psoriasis Scalp Severity Index (PSSI-75) relative to Day 0. Psoriasis must have affected $\geq 30\%$ of the scalp and the scalp psoriasis must have had erythema, desquamation, or induration. Secondary endpoints evaluated efalizumab's efficacy by PSSI-75 and PSSI-50; the proportion of patients achieving a Physician Global Assessment (PGA) rating of clear (0), almost clear (1), or mild (2); Scalpdex (a quality-of-life instrument for scalp dermatoses); and an assessment of patient-reported scalp itch.

Results: Ninety-nine subjects were enrolled. Ten subjects had unevaluable data, so 89 patients—62 in the efalizumab arm and 27 in the placebo arm—were included in ITT analyses. After 12 weeks, 77 (86.5%) patients remained enrolled—55 (88.7%) in the efalizumab arm and 22 (81.2%) in the placebo arm. The study did not meet the primary endpoint of PSSI-75 (p -value=0.1054); estimated response rates were 27.4% for efalizumab and 11.1% for placebo. The secondary endpoint involving scalp is consistent with the primary endpoint. No new safety signals were attributed to efalizumab.

Conclusions: At 12 weeks in this small study, the primary efficacy endpoint was not met. There was a non-statistically significant trend that would require a larger study to confirm. This presentation will include data from the 2nd 12-week course and the followup period.

Commercial Support: Funding support was provided by Genentech, Inc.

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P2319

Consistency of ustekinumab response across different body regions and PASI components for the treatment of moderate-to-severe psoriasis: Results from the PHOENIX 1 and PHOENIX 2 trials

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Background: The Psoriasis Area and Severity Index (PASI) score is useful as a composite measure of overall psoriasis disease severity based on body surface area (BSA) of involvement and extent of plaque induration, scale, and erythema. However, the degree to which the disease affects different regions of the body or different symptoms in an individual patient (pt) can vary.

Objective: To describe the efficacy of ustekinumab (UST) across different body regions and in each individual component of the PASI in psoriasis pts.

Methods: In two controlled Phase 3 clinical trials, PHOENIX 1 (n=766) and PHOENIX 2 (n=1230) pts with moderate-to-severe plaque psoriasis ($\geq 10\%$ of total BSA and PASI score ≥ 12) who were candidates for phototherapy or systemic therapy were randomized to SC UST 45mg or 90mg, or placebo (PBO), at wks 0 and 4. The primary endpoint was the proportion of pts achieving at least 75% improvement from baseline in the overall PASI (PASI75) score at wk12. PASI response was also assessed in each of the body regions evaluated (head, trunk, upper extremities, lower extremities) and for each of the PASI components (induration, scaling, erythema) at wk12.

Results: At wk12, significantly higher proportions of pts treated with UST 45mg and 90mg achieved an overall PASI75 response vs. PBO (PHOENIX 1: 67.1%, 66.4% vs. 3.7% and PHOENIX 2: 66.7%, 75.7% vs 3.7% for the 45mg, 90mg, and PBO groups, respectively ($p \leq 0.001$ for all comparisons). The proportions of pts in the combined UST vs. PBO groups achieving at least 75% improvement at wk12 for each body region were: 74.2% vs. 13.7% for the head, 70.3% vs. 4.8% for the trunk, 69.0% vs. 3.9% for the upper extremities, and 63.2% vs. 3.9% for the lower extremities (PHOENIX 1) and 77.6% vs. 10.3% for the head, 73.3% vs. 6.0% for the trunk, 72.4% vs. 2.9% for the upper extremities, and 68.8% vs. 3.7% for the lower extremities (PHOENIX 2). Consistent results were also observed in each of the individual components of the PASI score. The proportions of pts achieving at least 75% improvement for the individual PASI components for the combined UST vs PBO groups in each of the trials were: 66.9% vs 2.7% for induration, 66.9% vs. 4.3% for scaling, and 64.8% vs. 2.7% for erythema (PHOENIX 1) and 73.3% vs. 3.7% for induration, 72.8% vs. 3.7% for scaling, and 69.0% vs. 4.1% for erythema (PHOENIX 2).

Conclusion: UST provides a consistent response across all evaluated body regions and in each component of the PASI score; these response are comparable to the overall global PASI75 response.

Commercial Support: Centocor sponsored study