ORIGINAL RESEARCH

# Secukinumab Provides Clearer Skin and Better Control on Patient-Reported Psoriasis Symptoms of Itching, Pain, and Scaling than Placebo and Etanercept

Bruce Strober, M.D., Ph.D.;[1] Bárður Sigurgeirsson, M.D.;[2] Georg Popp, M.D.;[3] Rodney Sinclair, M.D.;[4] James Krell, M.D.;[5] Sigitas Stonkus, M.D.;[6] Marcis Septe, M.D.;[7] Boni E. Elewski, M.D.;[8] Alice B. Gottlieb, M.D., Ph.D.;[9] Yang Zhao, Ph.D.;[10] Vivian Herrera, M.Ph.;[10] Margaret Mordin, M.S.;[11] Dawn Odom, M.S.;[12] Charis Papavassilis;[13] Judit Nyirady, M.D.;[10] Mark Lebwohl, M.D.[14]

## ABSTRACT

**Background:** Secukinumab, a fully human anti-interleukin 17A monoclonal antibody, has demonstrated rapid, strong, and sustained efficacy in moderate-to-severe plaque psoriasis. **Objective:** To measure treatment effect on psoriasis-related itching, pain, and scaling during the first 12 weeks of treatment. **Methods:** ERASURE and FIXTURE were double-blind, multicenter, phase 3 studies in adults randomly assigned to secukinumab (300 mg or 150 mg), placebo, or etanercept (FIXTURE only). Improvements in itching, pain, and scaling and their bothersomeness, proportions of responders and proportions reporting complete symptom relief were compared. **Results:** Subjects treated with secukinumab reported significantly greater symptom improvement versus etanercept and placebo as well as bothersomeness reduction (all $P < 0.01$). The proportion of symptom responders and proportions reporting complete relief favored secukinumab. **Limitations:** Approximately 39% of patients provided data on psoriasis-related itching, pain, and scaling. **Conclusions:** Secukinumab significantly improves patient-reported itching, pain, and scaling compared with etanercept and placebo over 12-week psoriasis treatment.

[1]University of Connecticut, Farmington, Connecticut, and Probity Medical Research, Waterloo, Ontario, Canada; [2]University of Iceland, Faculty of Medicine, Department of Dermatology; [3]Licca Clinical Research Institute, Augsburg, Germany; [4]University of Melbourne, Melbourne, Australia; [5]Total Skin and Beauty Dermatology Center, Birmingham, Alabama; [6]A. Navickas Outpatient Clinic, Klaipeda, Lithuania; [7]Ventspils Poliklınika, Latvia; [8]University of Alabama at Birmingham, Birmingham, Alabama; [9]Tufts University School of Medicine, Boston, Massachusetts; [10]Novartis Pharmaceuticals Corporation, East Hanover, New Jersey; [11]RTI Health Solutions, Ann Arbor, Michigan; [12]RTI Health Solutions, Research Triangle Park, North Carolina; [13]Novartis Pharma AG, Basel, Switzerland; [14]Icahn School of Medicine at Mount Sinai, New York, New York

**Corresponding Author**
Margaret Mordin, M.S.
RTI Health Solutions
3005 Boardwalk Street, Suite 105
Ann Arbor, Michigan 48108
Tel: 703.483.9009
E-mail: mmordin@rti.org

**Funding Source:** Novartis Pharmaceuticals

**Conflict(s) of Interest**
Dr. Strober has served as a speaker, consultant, or investigator for AbbVie, Amgen, Celgene, Dermira, Janssen, Leo, Eli Lilly, Maruho, Medac, Merck, Novartis, Pfizer, Stiefel/GlaxoSmithKline, and UCB Pharma; as a Scientific Director for CORRONA Psoriasis Registry; and receives grant support through the University of Connecticut from AbbVie and Janssen. Dr. Sigurgeirsson has been a consultant for Novartis and received investigator and speaker fees. Dr. Popp has participated as aninvestigator for Novartis. Dr. Sinclair has participated as an investigator for Novartis. Dr. Krell has participated as an investigator, speaker, or consultant for Novartis, AbbVie, Merck, Janssen, and Amgen. Dr. Stonkus has participated as an investigator for Novartis. Dr. Septe has participated as an investigator for Novartis, LEO Pharma, AMAG Pharmaceuticals, AMGEN AB, Actelion Pharmaceuticals, Mitsubishi Pharma Europe, and Intendis GmbH. Dr. Elewski has served as a consultant for Novartis and Pfizer and has received research grants to the University Alabama from Amgen, AbbVie, Eli Lilly and Company, Merck, Novartis, and Pfizer. Dr. Gottlieb has consulted or served on advisory boards for Abbott Labs (AbbVie), Actelion, Akros, Amgen Inc., Astellas, Beiersdorf Inc., Bristol Myers Squibb Co., Canfite, Catabasis, Celgene Corp., Centocor (Janssen) Inc., Coronado, CSL Behring Biotherapies for Life, Dermipsor Ltd., DUSA, Eli Lilly and Company,

*Continued on page 168*

**Key words:** psoriasis, secukinumab, patient-reported outcome, itching, pain, scaling, bothersomeness, Psoriasis Symptom Diary

**Conflict(s) of Interest continued**

GlaxoSmithKline, Incyte, Karyopharm, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, TEVA, UCB, Vertex, and Xenoport; and has received research/educational grants (paid to Tufts Medical Center) from Abbott Labs (AbbVie), Amgen, Celgene, Centocor (Janssen), Coronado, Eli Lilly and Company, Levia, Merck, Novartis, Pfizer, and Xenoport. She has consulted or served on advisory boards through Tufts Medical Center for Amgen Inc.; Astellas, Akros, Centocor (Janssen), Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbott Labs. (Abbvie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma Co., Ltd, Takeda, Mitsubishi Tanabe Pharma Development America, Inc, Genentech, and Baxalta. Dr. Gottlieb has participated in research/educational grants through Tufts Medical Center for Centocor (Janssen), Amgen, Abbott (AbbVie), Novartis, Celgene, Pfizer, Lilly, Coronado, Levia, Merck, Xenoport, Dermira, and Baxalta. Dr. Zhao and Dr. Herrera are full-time employees of Novartis Pharmaceuticals, USA. Ms. Mordin and Ms. Odom are full-time employees of RTI Health Solutions. Dr. Papavassilis is a full-time employee of Novartis Pharma AG, Switzerland. Dr. Nyirady is a full-time employee of Novartis Pharmaceuticals Corporation, USA. Dr. Lebwohl is an employee of Mount Sinai Medical Center, which receives research funds from AbGenomics, AbbVie, Amgen, Anacor, Aqua, Canfite Biopharma, Celgene, Clinuvel, Coronado Biosciences, Ferndale, Lilly, Janssen Biotech, LEO Pharmaceuticals, Merz, Novartis, Pfizer, Sandoz, Sun Pharmaceuticals, and Valeant.

## INTRODUCTION

Psoriasis is a chronic immune-mediated skin condition characterized by patches of raised, erythematous plaques, often covered by silvery-white scales. Although most frequently forming on the elbows, knees, lower back, and scalp, these lesions can occur anywhere on the body.[1] Moderate-to-severe plaque psoriasis has a substantial impact on health-related quality of life.[2,3] Patients experience varying levels of symptom severity and a diverse symptom spectrum, usually localized to the lesions. Specifically, itching, pain, and scaling are often experienced by patients with chronic plaque psoriasis and reported to be highly bothersome.[3,4,5]

Although many patients may be treated with topical therapy, those with extensive (moderate to severe) psoriasis eventually require systemic or biologic therapy to modulate the immune response.[6] In two patient surveys, substantial proportions of patients reported being frustrated (40%) or dissatisfied (24-42%) with traditional therapies.[7] Newer biologic therapies may provide safe and more effective alternatives to conventional systemic agents for the treatment of moderate-to-severe psoriasis.[8]

Secukinumab, a fully human monoclonal antibody that selectively targets IL-17A, has been demonstrated in phase 3 studies to be highly efficacious in the treatment of moderate-to-severe plaque psoriasis, with an early onset, sustained efficacy, and favorable safety profile.[9,10] Psoriasis clinical improvement in skin clearance was assessed by the Psoriasis Area and Severity Index (PASI), with PASI 75 representing a 75-100% reduction and PASI 90 representing a 90-100% reduction in PASI score from baseline. Treatment with secukinumab (300 mg and 150 mg) resulted in high PASI 75 response rates at Week 12 (primary endpoint) for both studies (ERASURE: 81.6% and 71.6%, respectively; FIXTURE: 77.1% and 67.0%, respectively). In addition to clinical measures of skin clearance, patient-reported, psoriasis-related itching, pain, and scaling were included as one of the secondary endpoints for the secukinumab phase 3 FIXTURE and ERASURE trials to provide an evaluation of patient-reported psoriasis symptoms.

These symptoms were assessed from baseline through Week 12, using the Psoriasis Symptom Diary (PSD), a measure designed for use in global clinical trials, with the specific aim of generating patient-reported endpoints to evaluate efficacy for a treatment targeting moderate-to-severe chronic plaque psoriasis.[4,11,12] The primary objective of this analysis was to confirm the clinically observed treatment response based on patient-reported symptoms (itching, pain, scaling) of secukinumab versus etanercept (FIXTURE only) and versus placebo in the treatment of moderate-to-severe chronic plaque psoriasis.

## METHODS

### Study Design

The current analysis pooled data from two randomized, double-blind, double-dummy, placebo-controlled, multicenter phase 3 trials (ERASURE and FIXTURE) designed to assess the efficacy and safety of subcutaneous secukinumab in patients with moderate-to-severe plaque psoriasis. Eligible subjects were randomly assigned into treatment arms stratified by geographical region and by body weight (< 90 kg or ≥ 90 kg). Figure 1 provides an overview of the study designs. Each study's design, implementation, and reporting were

in accordance with the International Conference on Harmonisation's Harmonised Tripartite Guidelines for Good Clinical Practice. Langley and colleagues provide additional study details and clinical outcomes.[10]

## Sample

The two phase 3 trials randomized a total of 2,044 patients (ERASURE [N = 738] and FIXTURE [N = 1,306].) To address the present objectives, the analysis sample was limited to subjects who completed the PSD at baseline and at least once post-baseline through the Week 12 treatment period. Inclusion and exclusion criteria are described in detail by Langley and colleagues.[10]

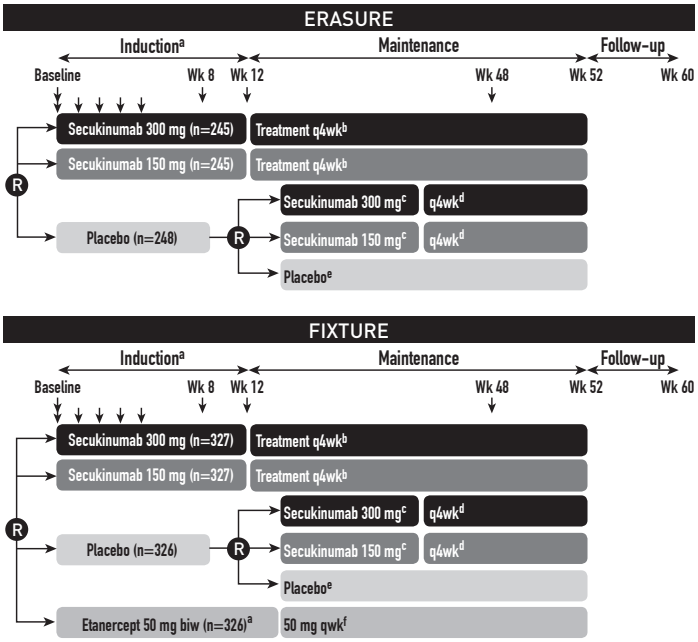
Although investigators and subjects were encouraged to complete the PSD, it was not mandatory, and translations were not available for two countries. Furthermore, due to customs delays, the electronic device used to administer the PSD was not available for two countries.

## Patient-Reported Outcomes

The PSD is a validated, 16-item, psoriasis-specific patient-reported outcome (PRO) measure with a 24-hour recall period (Appendix Table; Appendix available in Online Supplement at www.psoriasis.org/jppa), developed in accordance with recommendations set forth in the U.S. Food and Drug Administration's (FDA's) guidance for PRO measures and completed electronically. Through the instructions and question wording, patients were instructed to consider psoriasis-related symptoms when completing the PSD. Seven items evaluate the key signs and symptoms of plaque psoriasis: itching, stinging, burning, pain from skin cracking, psoriasis-related pain, scaling, and altered skin color. The remaining items assessed patient-reported bother associated with these signs and symptoms and daily impacts. Item responses are provided on a 0-10 rating scale, with higher scores indicating more severe symptoms or bother. This analysis focused on the itching, pain, and scaling items (items 1, 9, and 11; as key secondary endpoints) and bothersomeness of these symptoms (items 2, 10, and 12).

A weekly average was computed for each item as the sum of the scored item over the course of the study week divided by the number of days on which

**Figure 1.** Psoriasis Study Designs for the ERASURE and FIXTURE Trials




q 4wk = every 4 weeks; R = randomization; biw = twice weekly; qwk = once weekly; wk = week.
a Treatment or placebo at baseline and Weeks 1, 2, 3, 4, and 8; short arrows indicate time points at which doses were given during induction period.
b Maintenance treatment started at Week 12 and continued q4wk until Week 48.
c Treatment at Weeks 12, 13, 14, and 15.
d Treatment q4wk from Week 16 until Week 48.
e Placebo at Weeks 12, 13, 14, and 15, then q4wk from Week 16 until Week 48.
f Treatment administered biw until Week 12 and then qwk until Week 48.

the item was completed (four completed days were required to derive a weekly score; one to three missed days, consecutive or nonconsecutive, were allowed). If fewer than four completed days were in a study week, the item scores were set to missing.

## Analytic Methods

A two-sided test with alpha = 0.05 was used unless otherwise specified. Because the pooled analyses are exploratory in nature, results were not adjusted for multiple comparisons.

Summary statistics for the mean scores from baseline to Week 12 were calculated for each item by treatment group. The change from baseline to Week 12 was analyzed via analysis of covariance (ANCOVA) models with covariates for treatment (all four groups), geographical region, body weight stratum, and baseline PSD itching, pain, and scaling symptom value or the symptom bothersomeness value. Differences between treatment groups were determined using least square means and t-tests using the pooled error term from the linear model.

**Table 1.** Patient Demographic and Clinical Characteristics at Baseline

| Demographics and Characteristics | Secukinumab 300 mg (n = 224) | Secukinumab 150 mg (n = 229) | Etanercept (n = 136) | Placebo (n = 225) |
|---|---|---|---|---|
| Male, n (%) | 140 (62.5%) | 151 (65.9%) | 97 (71.3%) | 160 (71.1%) |
| Age, mean (SD) | 43.0 (13.1) | 45.7 (12.9) | 43.8 (13.0) | 43.1 (11.7) |
| Body weight (< 90 kg), n (%) | 121 (54.0%) | 128 (55.9%) | 89 (65.4%) | 124 (55.1%) |
| Body weight, mean (SD) | 90.3 (23.1) | 89.3(22.2) | 87.6 (21.7) | 89.5 (23.3) |
| PASI | | | | |
| Mean (SD) | 21.9 (9.0) | 21.8 (9.0) | 21.3 ( 8.0) | 21.6 (8.7) |
| Range | 12.0-64.2 | 12.0-69.6 | 12.0-49.6 | 10.6-50.2 |
| IGA | | | | |
| Moderate (level = 3), n (%) | 141 (63.0%) | 152 (66.4%) | 87 (64.0%) | 138 (61.3%) |
| Severe (level = 4), n (%) | 83 (37.1%) | 77 (33.6%) | 49 (36.0%) | 87 (38.7%) |
| PSD | | | | |
| Itching, mean (SD) | 6.4 (2.4) | 6.5 (2.4) | 6.2 (2.42) | 6.1 (2.5) |
| Pain, mean (SD) | 5.5 (3.0) | 5.3 (3.1) | 5.3 (2.96) | 5.0 (3.0) |
| Scaling, mean (SD) | 6.4 (2.6) | 6.5 (2.4) | 6.3 (2.61) | 6.2 (2.4) |
| Reporting no itching, n (%) | 1 (0.5%) | 2 (0.9%) | 2 (1.5%) | 2 (0.9%) |
| Reporting no pain, n (%) | 19 (8.5%) | 19 (8.3%) | 14 (10.3%) | 26 (11.6%) |
| Reporting no scaling, n (%) | 1 (0.5%) | 1 (0.4%) | 3 (2.2%) | 0 (0%) |
| Bothersomeness of itching, mean (SD) | 6.5 (2.53) | 6.4 (2.48) | 6.1 (2.52) | 6.0 (2.62) |
| Bothersomeness of pain, mean (SD) | 5.6 (3.056) | 5.34 (3.14) | 5.3 (3.02) | 5.0 (3.14) |
| Bothersomeness of scaling, mean (SD) | 6.4 (2.78) | 6.45 (2.61) | 6.2 (2.78) | 6.1 (2.70) |

*IGA = Investigator's Global Assessment modified 2011; PASI = Psoriasis Area and Severity Index; PSD = Psoriasis Symptom Diary (0-10 numerical rating scale via daily diary); SD = standard deviation.*

The proportion of psoriasis-related itching, pain, and scaling responders from Week 1 to Week 12 was compared by treatment using a Cochran-Mantel-Haenszel test stratified by geographic region and body weight. For this analysis, prespecified responder thresholds identified in the PSD psychometric evaluation using phase 2 data were applied: ≥ 2.2 points for itching, ≥ 2.2 for pain, or ≥ 2.3 for scaling, respectively from baseline.[11] Weekly proportion of subjects reporting complete symptom relief (responses of "no itching," "no pain," "no scaling" defined as a weekly average value of less than 0.5 on the 0-10 scale) and complete relief of the symptom bothersomeness (responses of "no bother" for itching, pain, and scaling defined as a weekly average value of less than 0.5 on the 0-10 scale) was reported by treatment groups.

# RESULTS

## Subject Characteristics

Of the 2,044 subjects who were randomly assigned, 39% (814/2044) completed the PSD at baseline and at least once during the 12-week induction phase. Descriptive statistics of demographics (i.e., gender, age) and clinical characteristics (body weight, PASI) were similar for those completing the PSD and those who did not complete the PSD (data not reported). Further, baseline demographics and disease characteristics were similar across treatment groups (Table 1) and similar to those previously reported in the overall trial population.[10] The mean age of subjects ranged from 43.0 years (secukinumab 300 mg group) to 45.7 years (secukinumab 150 mg group). Mean PASI scores at baseline were 21.9, 21.8, 21.3, and 21.6 for the secukinumab 300 mg, secukinumab 150 mg, etanercept, and placebo groups, respectively. Baseline mean itching, pain, and scaling scores (range, 5.0-6.5) and bothersomeness scores (range, 5.0-6.5) were similar across groups; all indicated moderate symptoms and bothersomeness. Furthermore, the baseline characteristics were similar for subjects who completed versus those who did not complete the PSD (mean age complete/non-complete = 44/45). Approximately 70% of participants in both groups were male.

## Itching, Pain, and Scaling Treatment Effect

Mean secukinumab symptom scores (left panel) quickly decrease (symptom improvement) over time, indicating quick and strong response to

**Table 2.** Changes from Baseline in Psoriasis Symptom Diary Pain, Itching, and Scaling and Symptom Bothersomeness at Week 12: LS Means

| Item | Secukinumab 300 mg (n = 224) | Secukinumab 150 mg (n = 229) | Etanercept (n = 136) | Placebo (n = 225) |
|---|---|---|---|---|
| Itching | | | | |
| Mean (SE) | 5.0 (0.17) | 4.7 (0.16) | 3.8 (0.21) | 0.6 (0.17) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | <0.0001 | |
| P value comparing with etanercept | < 0.0001 | < 0.0001 | | |
| Pain | | | | |
| Mean (SE) | 4.3 (0.17) | 4.0 (0.16) | 3.3 (0.21) | 0.4 (0.16) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | < 0.0001 | |
| P value comparing with etanercept | < 0.0001 | 0.0066 | | |
| Scaling | | | | |
| Mean (SE) | 5.1 (0.17) | 4.7 (0.16) | 3.6 (0.21) | 0.4 (0.17) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | < 0.0001 | |
| P value comparing with etanercept | < 0.0001 | < 0.0001 | | |
| Bothersomeness of itching | | | | |
| Mean (SE) | 5.0 (0.18) | 4.7 (0.18) | 3.7 (0.23) | 0.6 (0.18) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | < 0.0001 | |
| P value comparing with etanercept | < 0.0001 | 0.0002 | | |
| Bothersomeness of pain | | | | |
| Mean (SE) | 4.3 (0.17) | 4.0 (0.16) | 3.3 (0.21) | 0.3 (0.17) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | < 0.0001 | |
| P value comparing with etanercept | < 0.0001 | 0.0048 | | |
| Bothersomeness of scaling | | | | |
| Mean (SE) | 5.1 (0.19) | 4.7 (0.18) | 3.5 (0.23) | 0.5 (0.18) |
| P value comparing with placebo | < 0.0001 | < 0.0001 | < 0.0001 | |
| P value comparing with etanercept | < 0.0001 | < 0.0001 | | |

*ANCOVA = analysis of covariance; LS = least square ; SD = standard deviation; SE = standard error. LS means from ANCOVA with treatment, region, weight and baseline score.*

*Note: Negative change = improvement.*

treatment (Figure 2). ANCOVA results for changes from baseline to Week 12 also favored secukinumab (Table 2). Subjects treated with secukinumab 300 mg or 150 mg reported significantly greater improvement versus etanercept and placebo for all three symptoms. The magnitude of improvements based on least square mean changes consistently favored 300 mg, then 150 mg, then etanercept, and finally with minimal change that includes a plateau for placebo as follows, respectively:

- Itching: –5.0, –4.7, –3.8, and –0.6
- Pain: –4.3, –4.0, –3.3, and –0.4
- Scaling: –5.1, –4.7, –3.6, and –0.4
- P < 0.01 for all comparisons of secukinumab vs etanercept or placebo

Results were similar for the PSD bothersomeness items as provided by visual inspection of unadjusted mean scores over time (Figure 2, right panel) and the adjusted results (Table 2). For bothersomeness, both secukinumab treatment groups showed statistically significant treatment improvements compared to etanercept and compared to placebo (paired comparisons) (P < 0.01 for all comparisons) (Table 2).

## Itching, Pain, and Scaling Response Rates

Figure 3 presents the percentage of subjects classified as itching, pain, and scaling responders by week for each treatment group. Starting at Week 2, significantly greater response rates of itching (achieving ≥ 2.2 points from baseline), pain (≥ 2.2 points), and scaling (≥ 2.3 points) were achieved for secukinumab versus placebo and secukinumab versus etanercept (except for pain: not significant for Weeks 9-12 for secukinumab 150 mg vs. etanercept) at the P <0.05 level stratified by region and weight. At Week 12, the percentage of responders for itching was 83.0% (186/224) for subjects in the secukinumab 300 mg group and

**Figure 2.** Psoriasis Symptom Diary Mean Scores of Itching, Pain, and Scaling and Bothersomeness by Treatment Group: Baseline to Week 12

*Note: PSD scores range from 0 to 10, with higher scores indicating more severe symptoms or bother. Figure provides unadjusted mean scores.*

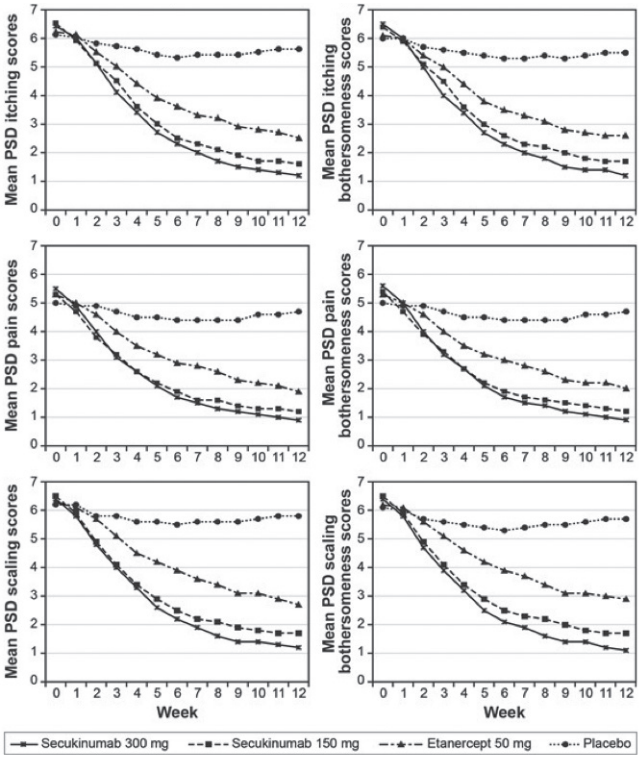
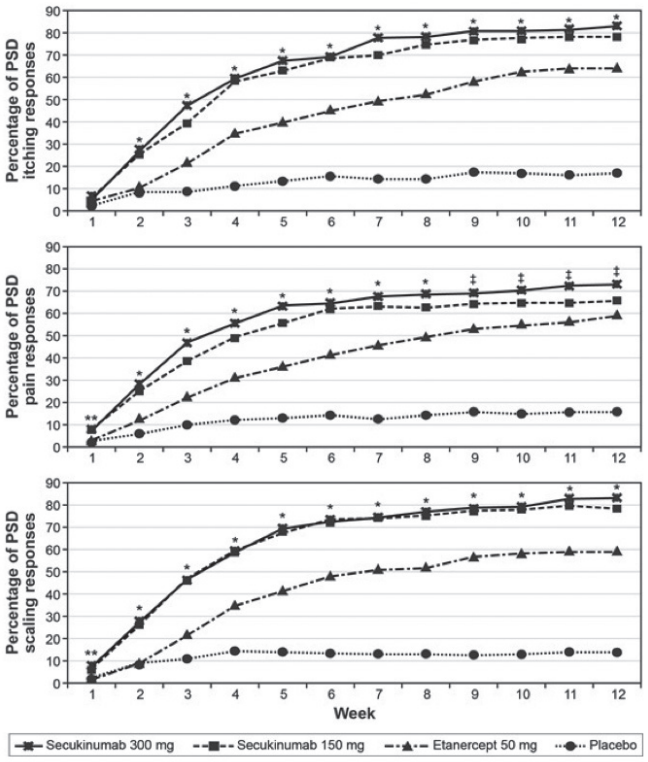



**Figure 3.** Psoriasis Symptom Diary Itching, Pain, Scaling Responder Rates – Week 1 to Week 12




PSD itching, pain, and scaling responders: Achieving at least the predetermined improvement/reduction of 2.2 points for itching, 2.2 points for pain, or 2.3 points for scaling from baseline on the weekly average of the 0-10 numerical rating scale.

** Secukinumab (300 mg, 150 mg) vs. placebo at $p < 0.05$ based on the Cochran-Mantel-Haenszel test stratified by region and weight.

* Secukinumab (300 mg, 150 mg) vs. placebo and secukinumab (300 mg, 150 mg) vs. etanercept significant at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight.

± Secukinumab (300 mg, 150 mg) vs. placebo and secukinumab 300 mg vs etanercept at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight.

78.2% (179/229) for subjects in the secukinumab 150 mg group versus 64.0% (87/136) for etanercept or 16.9% (38/225) for placebo subjects. Similarly, at Week 12, the percentage of responders for pain was 72.8% (163/224) for subjects in the secukinumab 300 mg group and 65.5% (150/229) for subjects in the secukinumab 150 mg group versus 58.8% (80/136) for etanercept or 15.6% (35/225) for placebo subjects. At Week 12, the percentage of responders for scaling was 83.0% (186/224) subjects in the secukinumab 300 mg group and 78.2% (179/229) for subjects in the secukinumab 150 mg group versus 58.8% (80/136) for etanercept or 13.8% (31/225) for placebo subjects.

## Itching, Pain, and Scaling Complete Relief Rates

Figure 4 presents the proportion of subjects classified as achieving complete symptom relief (reporting no itching, pain, or scaling, respectively) and complete relief of symptom bothersomeness (reporting no bothersomeness of itching, pain, or scaling, respectively) by week for each treatment group. Starting as early as week four for scaling and week six for itching and pain, significantly greater rates of complete relief were achieved for secukinumab versus placebo and secukinumab versus etanercept at the $p < 0.05$ level stratified by region and weight. The largest proportion of complete relief at Week 12 was reported for pain at 58.5% (131/224) for 300 mg, 52.8% (121/229) for 150 mg, 35.3% (48/136) for etanercept, and 10.7% (24/225) for placebo. Comparisons on the proportion of itching and scaling complete relief (Week 12 secukinumab 300 mg, etanercept, placebo itching: 43.8%, 25.0%, 1.8%, respectively, and scaling: 42.0%, 20.6%, 1.8%, respectively) favored secukinumab 300 mg. Results were similar for bothersomeness. The largest proportion reporting no bothersomeness at Week 12 was for pain at 60.7% (136/224) for 300 mg, 53.7% (123/229) for 150 mg, 36.8% (50/136) for etanercept, and 11.1% (25/225) for placebo.

## DISCUSSION AND CONCLUSIONS

The present analysis assessed the effect of secukinumab treatment on three key patient-reported symptoms (itching, pain, and scaling) by the PSD. The itching, pain, and scaling items were able to detect rapid improvements in symptom response as early as Week 2 and were sensitive enough to discern differences in response between two biologic treatments (secukinumab and etanercept). Greater proportions of subjects treated with secukinumab achieved response threshold for itching, pain, and scaling relative to etanercept and placebo. Furthermore, complete symptom relief and relief of bothersomeness of these three symptoms favored secukinumab treatment versus etanercept and secukinumab versus placebo. This analysis indicates that secukinumab therapy is an important advance, with benefits to patients on both clinical and self-reported improved symptoms with a favorable safety profile.

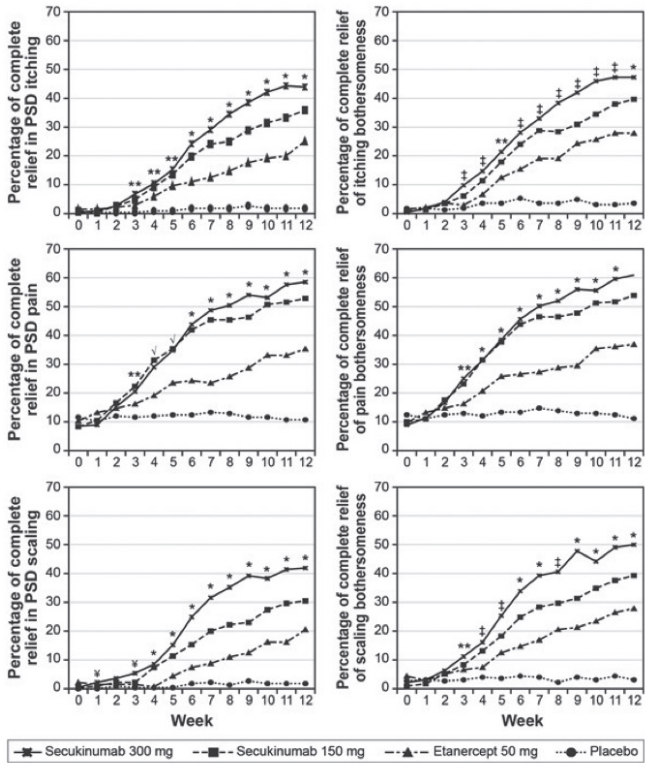

## ACKNOWLEDGEMENTS

The authors would like to thank the subjects and the investigators who participated in the studies.


## REFERENCES


1. Van Voorhees A, Feldman SR, Koo J, et al. The psoriasis and psoriatic arthritis pocket guide. 2009. Available at: http://psoriasis.org/health-care-providers/treating-psoriasis. Accessed 4 May 2015.
2. de Korte J, Sprangers MA, Mombers FM, Bos JD. Quality of life in patients with psoriasis: a systematic literature review. J Investig Dermatol Symp Proc. 2004;9:140-147.
3. Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. J Am Acad Dermatol. 2014 May;70(5):871-881.
4. Lebwohl M, Swensen AR, Nyirady J, et al. The Psoriasis Symptom Diary: development and content validity of a novel patient-reported outcome instrument. Int J Dermatol. 2014 Jun;53(6):714-722.
5. Martin ML, McCarrier KP, Chiou CF, et al. Early development and qualitative evidence of content validity for the Psoriasis Symptom Inventory (PSI), a patient-reported outcome measure of psoriasis symptom severity J Dermatolog Treat. 2013 Aug;24(4):255-260.
6. Mrowietz U, Kragballe K, Reich K, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res. 2011 Jan;303(1):1-10.
7. Raval K, Lofland JH, Waters H, Piech CT. Disease and treatment burden of psoriasis: examining the impact of biologics. J Drugs Dermatol. 2011 Feb;10(2):189-196.
8. Sterry W, Barker J, Boehncke WH, et al. Biological therapies in the systemic management of psoriasis: international consensus conference. Br J Dermatol. 2004:151(Suppl. 69):3-17.
9. Novartis Pharma AG. Consentyx prescribing information. 2015. Available at: http://www.pharma.us.novartis.com/product/pi/pdf/cosentyx.pdf. Accessed 23 February 2015.
10. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in Plaque Psoriasis: Results of Two Phase 3 Trials. N Engl J Med. 2014 Jul 24;371(4):326-338.
11. Strober B, Gottlieb AB, Elewski B, et al. Item-level psychometric properties for a new patient-reported symptom diary. Value Health. 2013;16:1014-1022.
12. Food and Drug Administration (FDA). Guidance for industry. Patient-reported outcome measures: use in medical product development to support labeling claims. December 2009. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf. Accessed 4 May 2015.


**Figure 4.** Psoriasis Symptom Diary Complete Relief Rates for Itching, Pain, and Scaling and Bothersomeness – Week 1 to Week 12




Complete relief: Responses of "no itching," "no pain," or "no scaling" as defined as a weekly value of less than 0.5 on the weekly average 0-10 numerical rating scale. Complete relief of the symptom bothersomeness: Responses of "no bother" for itching, pain, and scaling as defined as a weekly value of less than 0.5 on the 0-10 scale.

** Secukinumab (300 mg, 150 mg) vs. placebo at $p < 0.05$ based on the Cochran-Mantel-Haenszel test stratified by region and weight.

* Secukinumab (300 mg, 150 mg) vs. placebo and secukinumab (300 mg, 150 mg) vs. etanercept significant at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight.

± Secukinumab (300 mg, 150 mg) vs. placebo and secukinumab 300 mg vs etanercept at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight. √ Secukinumab (300 mg, 150 mg) vs. placebo and secukinumab 150 mg vs etanercept at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight.

¥ Secukinumab 300 mg vs. placebo at $p < 0.05$ based on Cochran-Mantel-Haenszel test stratified by region and weight.

Appendix a

**Table 1.** The 16-Item Psoriasis Symptom Diary

| Item Stem | Response Anchors, 0-10 Numerical Rating Scale |
|---|---|
| 1. Overall, how severe was your psoriasis-related itching over the past 24 hours? | 0 = No itching<br>10 = Itching as bad as you can imagine |
| 2. Overall, how bothered were you by your psoriasis-related itching over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 3. Overall, how severe was your psoriasis-related stinging over the past 24 hours? | 0 = No stinging<br>10 = Stinging as bad as you can imagine |
| 4. Overall, how bothered were you by your psoriasis-related stinging over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 5. Overall, how severe was your psoriasis-related burning over the past 24 hours? | 0 = No burning<br>10 = Burning as bad as you can imagine |
| 6. Overall, how bothered were you by your psoriasis-related burning over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 7. Overall, how severe was the pain from your psoriasis-affected skin cracking over the past 24 hours? | 0 = No pain<br>10 = Pain as bad as you can imagine |
| 8. Overall, how bothered were you by the pain from your psoriasis-affected skin cracking over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 9. Overall, how severe was your psoriasis-related pain over the past 24 hours? | 0 = No pain<br>10 = Pain as bad as you can imagine |
| 10. Overall, how bothered were you by your psoriasis-related pain over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 11. Overall, how severe was your psoriasis scaling over the past 24 hours? | 0 = No scaling<br>10 = Scaling as bad as you can imagine |
| 12. Overall, how bothered were you by your psoriasis scaling over the past 24 hours? | 0 = Not bothered at all<br>10 = Bothered as bad as you can imagine |
| 13. Overall, how noticeable did you think the color of your psoriasis-affected skin was over the past 24 hours? | 0 = Not at all noticeable<br>10 = Noticeable as bad as you can imagine |
| 14. Overall, how much did you try to hide your psoriasis-affected skin over the past 24 hours? | 0 = Did not try to hide at all<br>10 = Totally avoided being seen by others |
| 15. Overall, how much did your psoriasis cause you to avoid activities with other people over the past 24 hours? | 0 = You did not avoid other people<br>10 = Avoided other people as much as you ever have |
| 16. Overall, how embarrassed were you because of your psoriasis over the past 24 hours? | 0 = No embarrassment<br>10 = Embarrassment as bad as you can imagine |

*Note: If 0 was selected for the "symptom" item, the corresponding "bother" item was not asked and was scored as 0.*