



Secukinumab Provides Rapid Relief From Itching and Pain in Patients with Moderate-to-Severe Psoriasis: Patient Symptom Diary Data from Two Phase 3, Randomized, Placebo-controlled Clinical Trials

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In patients with psoriasis, severe itching of the skin and pain are among the most bothersome symptoms of the disease (1). Itching is one of the most prevalent symptoms, affecting >75% of patients with psoriasis (2, 3), whereas pain has been reported in approximately 45% of patients with psoriasis (3). For many patients, the presence of severe itching is associated with increased disease severity, reduced health-related quality of life and work productivity, and decreased psychosocial well-being (4, 5). Patient symptoms are often underestimated; therefore, treatments that address all aspects of the disease, including rapid and sustained improvement in itching and pain, are critical for improving the overall quality of life of patients with psoriasis.

Secukinumab is a fully human monoclonal antibody that selectively neutralizes interleukin 17A, a cornerstone cytokine involved in the development of psoriasis. Secukinumab has shown long-lasting efficacy and safety in the complete spectrum of psoriasis manifestations, including nails, scalp, palmoplantar, and psoriatic arthritis (6–12). A previous analysis of pooled Psoriasis Symptom Diary (PSD) data from the ERASURE (NCT01365455) and FIXTURE (NCT01358578) pivotal studies showed that treatment with secukinumab resulted in significant improvements in patient-reported psoriasis-related itching, pain, and scaling symptoms at week 12 compared with placebo (13). This report highlights the effectiveness of secukinumab in achieving rapid improvements in patient-reported itching and pain within the first 4 weeks of treatment using pooled PSD data from the randomized, double-blind, placebo-controlled, phase 3 ERASURE and FIXTURE clinical trials.

METHODS AND RESULTS

Full details of the study designs and patient enrollment criteria for ERASURE and FIXTURE have been described previously (6). Patient-reported itching and pain were assessed during the first 12 weeks of treatment using the PSD, a validated and responsive tool designed to capture the daily signs and symptoms of psoriasis reported by the patient, based on 16 items evaluating psoriasis-related characteristics (1, 14). The results reported here focus on severity of psoriasis-related itching and pain over the past 24 h, on a scale from 0 (no itching/pain) to 10 (itching/pain as bad as you can imagine) (1).

Weekly means for the PSD categories of itching and pain were derived during the induction treatment period (weeks 1–12), defined as the sum of the scored item over the course of the week divided by the number of days on which the item was completed. Values were designated as missing if ≥ 4 daily assessments

were missing for the corresponding question. Missing values were imputed using the last observation carried forward method. The absolute change in itching and pain scores from baseline to weeks 2, 4, and 12 were compared across treatment groups using analysis of covariance. The proportion of patients within each treatment arm who achieved no or minimal itching/pain (score of 0 or 1) was also assessed weekly and compared across treatment groups to examine trends over time in the proportion of patients who remained with no or minimal itching/pain. The proportions of patients who achieved different thresholds of improvement (i.e., no improvement or improvement ≤ 2 points, >2 to 3 points, >3 to 5 points, or >5 points) at week 12 were also assessed (14). All analyses were for hypothesis generation only. No adjustment was made for multiple comparisons.

Among the 40.2% of patients (820/2,042) who completed the PSD at baseline, baseline demographics and disease characteristics were similar across all treatment groups and were consistent with analyses previously published from FIXTURE and ERASURE (Table S1^a) (6, 13).

Patients treated with secukinumab demonstrated rapid improvements in itching severity, with mean improvements in scores from baseline observed as early as week 2 in both secukinumab dose groups (150 mg, -1.36 ; 300 mg, -1.38) that were significantly greater than those with placebo (-0.25) and etanercept (-0.69). Significantly greater improvements from baseline were also observed at week 4 in both secukinumab dose groups (150 mg, -2.87 ; 300 mg, -3.03) compared with placebo (-0.42) and etanercept (-1.86) ($p < 0.05$ for all comparisons vs placebo and etanercept) (Fig. S1a¹). The improvements in itching scores were maintained through week 12 in the secukinumab dose groups (150 mg, -4.90 ; 300 mg, -5.14) relative to placebo (-0.40) and etanercept (-3.80).

Similarly, improvements in pain were reported as early as week 2 in both secukinumab dose groups (150 mg, -1.48 ; 300 mg, -1.55) compared with placebo (-0.07) and etanercept (-0.74), with significantly greater improvements also observed at week 4 in both secukinumab dose groups (150 mg, -2.65 ; 300 mg, -2.92) compared with placebo (-0.28) and etanercept (-1.81) ($p < 0.05$ for all comparisons vs placebo and etanercept; Fig. S1b¹). The improvements in pain scores with secukinumab treatment were maintained through week 12 in both dose groups (150 mg, -4.02 ; 300 mg, -4.52) relative to placebo (-0.16) and etanercept (-3.48).

At week 2, the proportion of patients who achieved no (0) or minimal (1) itching was significantly greater with secukinumab 300 mg than with placebo (6.0% vs 1.4%; $p < 0.05$), and numerical improvements were observed with both secukinumab doses vs etanercept (Fig. S1c¹). At week 4, the proportions of patients who achieved no/minimal itching were significantly greater with secukinumab 150 and 300 mg than with placebo (14.5% and 19.4% vs 2.4%; $p < 0.05$); secukinumab 300 mg also showed significant improvements vs etanercept (19.4% vs 9.0%; $p < 0.05$). Similar trends were observed with improvements in patient-reported pain

¹<https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3195>

severity (Fig. S1d¹). At week 12, the proportions of patients who achieved no or minimal itching and pain, respectively, were significantly higher in both secukinumab dose groups (150 mg, 57.2% and 64.6%; 300 mg, 68.6% and 72.4%) than in the etanercept (39.8% and 48.0%) and placebo (4.2% and 6.3%) groups ($p < 0.05$ for all comparisons vs placebo and etanercept).

Patients receiving secukinumab were numerically more likely to achieve improvements from baseline in itching (Fig. S2a¹) and pain severity (Fig. S2b¹) scores of > 5 points at week 12 compared with patients receiving etanercept or placebo.

DISCUSSION

In this pooled analysis of two pivotal phase 3 trials in moderate-to-severe psoriasis, secukinumab demonstrated significantly greater improvements from baseline in patient-reported itching and pain as early as week 2 compared with placebo and etanercept; these improvements were maintained throughout the induction period (week 12). This is the first report demonstrating rapid and significant relief in itching and pain after only 2 weeks of treatment in patients with moderate-to-severe plaque psoriasis. The speed and robustness of improvement in patient-reported symptoms align with objective measures from FIXTURE and ERASURE, which showed that approximately 40% and 20% of patients receiving secukinumab 300 and 150 mg, respectively, achieved PASI75 responses at week 4 (6).

Although the PSD was completed by only approximately 40% of patients enrolled in the FIXTURE and ERASURE trials, their demographic and clinical characteristics were similar to those of the overall study population (13); therefore, these findings may be generalizable to a wider moderate-to-severe psoriasis population. Taken together, these findings show that secukinumab can provide early relief from psoriasis-related itching and pain, which may also improve overall quality of life (15). These results are critical to understanding the effects of psoriasis on patients' lives and the importance of rapid onset and durability of treatment in providing relief of bothersome symptoms from a patient perspective.

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REFERENCES

- Lebwohl M, Swensen AR, Nyirady J, Kim E, Gwaltney CJ, Strober BE. The Psoriasis Symptom Diary: development and content validity of a novel patient-reported outcome instrument. *Int J Dermatol* 2014; 53: 714–722.
- Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL. The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 2000; 143: 969–973.
- Korman NJ, Zhao Y, Li Y, Liao M, Tran MH. Clinical symptoms and self-reported disease severity among patients with psoriasis – implications for psoriasis management. *J Dermatolog Treat* 2015; 26: 514–519.
- Ljosaa TM, Mork C, Stubhaug A, Moum T, Wahl AK. Skin pain and skin discomfort is associated with quality of life in patients with psoriasis. *J Eur Acad Dermatol Venereol* 2012; 26: 29035.
- Korman NJ, Zhao Y, Pike J, Roberts J, Sullivan E. Increased severity of itching, pain, and scaling in psoriasis patients is associated with increased disease severity, reduced quality of life, and reduced work productivity. *Dermatol Online J* 2015; 21. pii: 13030/qt1x16v3dg.
- Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, et al; ERASURE Study Group; FIXTURE Study Group. Secukinumab in plaque psoriasis – results of two phase 3 trials. *N Engl J Med* 2014; 371: 326–338.
- Blauvelt A, Prinz JC, Gottlieb AB, Kingo K, Sofen H, Ruer-Mulard M, et al; FEATURE Study Group. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE). *Br J Dermatol* 2015; 172: 484–493.
- Paul C, Lacour JP, Tedremets L, Kreutzer K, Jazayeri S, Adams S, et al; JUNCTURE study group. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). *J Eur Acad Dermatol Venereol* 2015; 29: 1082–1090.
- Thaci D, Blauvelt A, Reich K, Tsai TF, Vanaclocha F, Kingo K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol* 2015; 73: 400–409.
- Armstrong AW, Vender R, Kircik L. Secukinumab in the treatment of palmoplantar, nail, scalp, and pustular psoriasis. *J Clin Aesthet Dermatol* 2016; 9: S12–S16.
- Mease P, van der Heijde D, Landewé R, Mpofu S, Rahman P, Tahir H, et al. Secukinumab improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III FUTURE 5 study. *Ann Rheum Dis* 2018; 77: 890–897.
- Bagel J, Germino R, Guana A, Herrera V, Greenberg JD, Litman HJ, et al. Secukinumab clinical and patient-reported outcomes after 1 year of follow-up: real-world analyses from the Corrona Psoriasis Registry. Presented at: 27th European Academy of Dermatology and Venereology Congress; September 12–16, 2018; Paris, France [ePoster P1850].
- Strober B, Sigurgeirsson B, Popp G, Sinclair R, Krell J, Stonkus S, et al. Secukinumab improves patient-reported psoriasis symptoms of itching, pain, and scaling: results of two phase 3, randomized, placebo-controlled clinical trials. *Int J Dermatol* 2016; 55: 401–407.
- Strober BE, Nyirady J, Mallya UG, Guettner A, Papavassilis C, Gottlieb AB, et al. Item-level psychometric properties for a new patient-reported psoriasis symptom diary. *Value Health* 2013; 16: 1014–1022.
- Stull DE, Griffiths CEM, Gilloteau I, Zhao Y, Guana A, Finlay AY, et al. Differential effects of secukinumab vs. ustekinumab for treatment of psoriasis on quality of life, work productivity and activity impairment: a structural equation modelling analysis. *Br J Dermatol* 2018; 178: 1297–1307.