Etanercept Improves Skin Lesions and Symptoms of Depression and Fatigue in Patients with Moderate to Severe Psoriasis

Tyring S, Gottlieb A, Papp K, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomized phase III trial. Lancet 2006;367:29–35.

Study Overview

Objective. To determine the effects of etanercept on symptoms of fatigue and depression associated with moderate to severe psoriasis.

Design. Randomized, double-blind, placebo-controlled trial with an intention-to-treat analysis.

Setting and participants. Participants were recruited from 39 sites in the United States and Canada and were eligible if they were aged ≥ 18 years; had active, clinically stable psoriasis with ≥ 10% total body surface area affected; had a Psoriasis Area and Severity Index (PASI) score ≥ 10; and had received or had been a candidate to receive previous phototherapy or systemic therapy for psoriasis. Patients were excluded if they had a history of psychiatric disease; a skin condition other than psoriasis; or active guttate, erythrodermic, or pustular psoriasis. 620 patients were randomized to etanercept (n = 311) 50 mg twice weekly or matching placebo (n = 309) for 12 weeks. Safety and efficacy were measured at baseline and then at weeks 1, 2, 4, 8, and 12.

Main outcome measures. The primary endpoint was a ≥ 75% improvement in PASI score from baseline to week 12. Secondary endpoints included improvements on several symptom assessment scales, including the Dermatology Life Quality Index (DLQI), the Functional Assessment of Chronic Illness Therapy Subscale Fatigue (FACIT-F), the Hamilton Depression Rating Scale (Ham-D), and the Beck Depression Inventory (BDI). Data on adverse and severe adverse events were also collected.

Main results. 292 placebo-treated patients and 305 etanercept-treated patients completed the study. Baseline characteristics were similar between the 2 groups. By week 12, 47% of etanercept-treated patients had a 75% improvement in PASI score compared with 5% of placebo-treated patients (difference, 42%; $P < 0.001$). 69% of patients in the etanercept group had improvements in the DLQI compared with 22.1% in the placebo group ($P < 0.001$). There were statistically significant improvements in both BDI and Ham-D scores at 12 weeks in the etanercept group compared with placebo, and etanercept-treated patients had a 5-point improvement on the FACIT-F compared with 1.9 points for placebo-treated patients ($P < 0.001$). 49% of etanercept-treated patients experienced at least 1 adverse event compared with 44.8% of placebo-treated patients.

Conclusion. Etanercept improves skin lesions and symptoms of fatigue and depression in patients with moderate to severe psoriasis.

Commentary

Psoriasis can be disabling not only because of the extensive skin involvement but also due to the severe psychologic stress often associated with this disease [1]. In 1 study, almost 80% of respondents noted that psoriasis had had a negative impact on their lives [2]. While prior studies have suggested that treatment of psoriasis can improve a patient's quality of life, few studies have evaluated whether treatment may alleviate the specific symptoms of depression. Etanercept, a tumor necrosis factor-α (TNF-α) receptor, works by inhibiting TNF-α binding to cell surface receptors and blocking cellular response to TNF-α. Tyring et al's well-designed randomized controlled trial contributes to a growing body of literature to support the use of anti-TNF-α therapy [3,4] by demonstrating that these agents may also reduce symptoms of depression and fatigue. A particular strength of Tyring et al's study is that

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several validated depression scales were used, and follow-up was close to 100%.

One challenge of interpreting studies that use survey scores as an outcome is determining whether the magnitude of change actually represents any clinical meaningful change. Although an increase of a few points on a specific scale may reach statistical significance, often it is unclear whether this difference translates into actual benefit for the patient. Tyring and colleagues considered a meaningful improvement for either the BDI or Ham-D to be a greater than 50% improvement from baseline. Although the results were statistically significant and more etanercept-treated patients had meaningful improvement, it is not clear from the data provided what percentage of patients had mild versus moderate to severe depression at 12 weeks compared with baseline. Because the range of scores is substantial in the moderate to severe category (BDI, 17–63; Ham-D, 18–53), a 50% reduction in score may not necessarily translate into a change in an individual's severity of depression. For the FACIT-F, a change of 3 points has previously been considered a significant improvement in fatigue, and this was the approximate magnitude of change observed in this study for the etanercept arm when compared with placebo.

Applications for Clinical Practice

Several trials have demonstrated that etanercept is effective at reducing skin lesions in psoriasis, but etanercept may also alleviate symptoms of fatigue and depression associated with moderate to severe psoriasis. Because depression and fatigue are commonly associated with psoriasis and directly influence patients' quality of life, this study should help provide the clinician with additional evidence to guide therapy selection.

–Review by Harvey J. Murff, MD, MPH

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