Etanercept Improves Psoriatic Arthritis Patient-Reported Outcomes: Results From EDUCATE

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Experience Diagnosing, Understanding Care, and Treatment With Etanercept (EDUCATE) is a multicenter, phase 4, 24-week, open-label study of the safety and efficacy of etanercept therapy in patients with psoriatic arthritis (PsA) in routine dermatologic practice. We present data on patient-reported outcomes (PROs) from EDUCATE, which demonstrate that subjects with PsA achieved clinically meaningful improvements in both skin- and joint-related PROs after 24 weeks of treatment.

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Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by skin and joint manifestations. The psoriatic skin lesions of PsA often are what prompts affected individuals to seek treatment from a dermatologist.[1] Psoriasis affects 1% to 3% of the population, and 5% to 42% of those individuals also will develop joint symptoms.[2] Involvement of the spine and sacroiliac, peripheral, and distal interphalangeal joints can be diagnostic for PsA. Although PsA can be mild and nondestructive, it has the potential to become destructive through bone lysis and joint ankylosis.[2]

PsA can be modulated by immunosuppressive therapy.[1] Therapies such as methotrexate and cyclosporine are effective for skin and joint symptoms but are not ideal for long-term use because of potential treatment toxicity. Therapies targeting specific cytokines are now available to modulate inflammatory disease. Etanercept, a soluble tumor necrosis factor receptor Fc fusion protein, has been shown to improve the signs and symptoms of PsA, inhibit the physical destruction and deformity of joints, and help maintain existing functional status in randomized clinical trials (RCTs).[3,4]

However, RCTs evaluate drug safety and efficacy on small frequently homogenous populations with highly active disease and may not accurately represent patients in general dermatology practice. The Experience Diagnosing, Understanding Care, and Treatment With Etanercept (EDUCATE) trial, a multicenter, phase 4, open-label study, complements RCT results by providing safety and efficacy data on etanercept use in patients with PsA in a dermatologic community setting. Better awareness of the incidence, signs, and symptoms of PsA might help distinguish this disease from psoriasis and initiate treatment earlier, thereby preventing disability and disease progression. Here, we evaluate the effects of etanercept therapy on patient-reported outcomes (PROs) in subjects from the EDUCATE trial.

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Methods

Subjects—Subjects with PsA from 125 dermatology clinics throughout the United States were enrolled in the EDUCATE trial (N=1122), and more than 83% of subjects were treated at community-based facilities. Institutional review boards at the participating sites approved the study protocol, and all subjects signed informed consent forms before study-related procedures began. Subject eligibility was similar to that in Mease et al,[5] except that EDUCATE defined active PsA more broadly to include a greater diversity of subjects with PsA (≥3 swollen joints and ≥3 tender/painful joints vs ≥2 swollen joints and ≥2 tender/painful joints for at least 3 months or either sacroiliitis or spondylitis in ≥1 joint, respectively). A detailed synopsis of EDUCATE and its eligibility requirements can be found at the Clinical Study Results Web site.[6]

Study Design—Subjects received etanercept 50 mg once weekly. The drug was self-administered as two 25-mg subcutaneous injections as directed,[7] beginning at baseline for 24 weeks. Evaluations were performed at baseline (week 0) and at weeks 2, 6, 12, and 24.

End Points—The Dermatology Life Quality Index (DLQI) measures patient disability related to dermatoses such as psoriasis.[8] The total DLQI value represents the sum of the scores for each of the 10 questions (maximum score=30). The 10 questions are grouped into 6 subscales (daily activities, personal relationships, leisure, work and school, treatment, and symptoms and feelings) that can be independently assessed. A reduction from baseline of 5 or more in the DLQI score is considered a minimal clinically important difference (MCID).[9]

The Patient Global Assessment of Psoriasis (Patient GA Psoriasis) and the Patient Itching Scale are 2 components of the National Psoriasis Foundation Psoriasis Score.[10] They are scored on a scale of 0 (best) to 5 (worst).

The Health Assessment Questionnaire Disability Index (HAQ DI) measures disability in activities of daily living.[11] The HAQ DI is composed of 8 subscales (hygiene, activities, reach, walking, eating, arising, grip, and dressing and grooming) assessing how joint disease affects functional status. Responses are scored on a scale of 0 to 3 (0=no disability in the activity tested and 3=completely disabled). Subscale scores are averaged to calculate a final value. The MCID for the HAQ DI for PsA is a 0.3 or more unit reduction.[12]

The Patient Global Assessment of Joint Disease (Patient GA Joint Disease) and Patient Global Assessment of Joint Pain (Patient GA Joint Pain) use patient-provided numeric assessments of the current status of disease. The scale for Patient GA Joint Disease is 0=no symptoms to 5=severe symptoms. The scale for the Patient GA Joint Pain is 0=no pain to 10=severe pain.

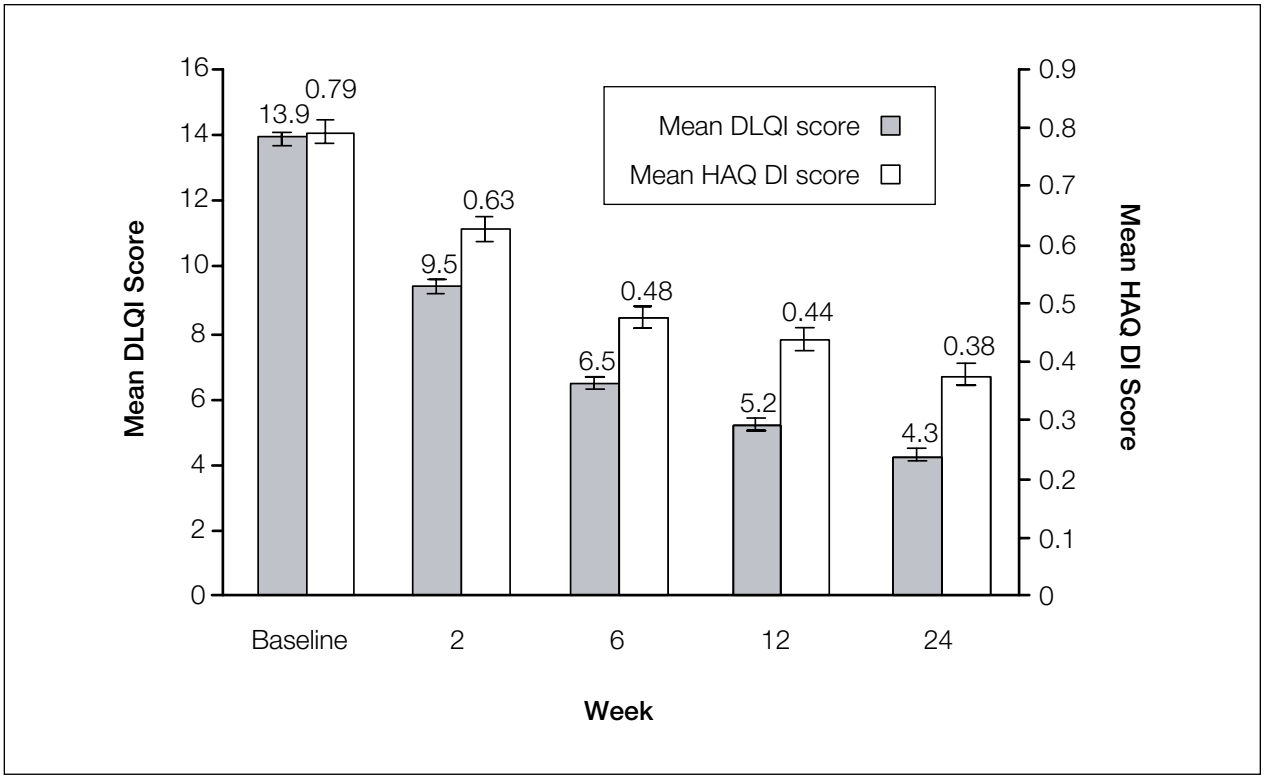
Statistical Methods—Subjects who received at least one dose of study drug are included in the analysis. Summary statistics were used to describe subject demographics and disease characteristics at baseline. Missing data points were imputed using the last observation carried forward method.

Results

Of the 1122 subjects enrolled, 1010 subjects (90%) completed the study. Subjects who withdrew from the study did so primarily because of loss to follow-up (3.4%), adverse event (2.1%), disease progression (1.4%), or consent withdrawal (1.2%). Of those enrolled, 54.5% of subjects were men, and 84.5% of subjects were white. The mean (SD) age was 48.0 (13.4) years, mean (SD) duration of psoriasis was 19.0 (12.9) years, and mean (SD) duration of PsA was 7.2 (8.3) years. At baseline, 79.7% of subjects had moderate to severe levels of psoriasis, and the mean (SD) percentage of body surface area affected by psoriasis was 26.8% (19.4). Regarding joint-related characteristics, baseline levels of disease were a mean (SD) tender/painful joint count of 9.9 (10.8) and a mean (SD) swollen joint count of 5.6 (7.2). Finally, 40.7% of enrollees had a history of sacroiliitis, and 30.4% had a history of spondylitis.

The DLQI, Patient GA Psoriasis, and Patient Itching Scale measure changes in physical and psychologic status. The mean baseline DLQI was 13.9. DLQI improvements were observed as early as 2 weeks after initiation of etanercept therapy when the mean DLQI score declined to 9.5, which constituted a 30% (95% CI, 28%−32%) mean percentage improvement from baseline (Figure). The mean score reduction in DLQI from baseline at 24 weeks was 9.6 (95% CI, 9.2−10.1), a mean percentage improvement from baseline of 66% (95% CI, 64%−69%). At 12 weeks, 72% (95% CI, 69%−74%) of subjects achieved an MCID of 5 or more, which was maintained by 76% (95% CI, 73%−78%) of subjects at 24 weeks. In addition, 22% of subjects achieved a DLQI score of 0 at 24 weeks.

Improvements in all DLQI subscales were similar to improvements observed for the total DLQI score. The percentage improvement from baseline scores ranged from 42% to 62% after 24 weeks. Etanercept treatment had the largest effect on the subscales of daily activities, leisure, and symptoms and feelings (62%, 61%, and 60% improvements



Mean Dermatology Life Quality Index (DLQI) scores and mean Health Assessment Questionnaire Disability Index (HAQ DI) scores during a 24-week course of etanercept therapy.

from baseline at 24 weeks, respectively). The subscales with the highest initial baseline scores also had the greatest percentage improvement from baseline.

Improvements in the Patient GA Psoriasis and Patient Itching Scale scores were similar to DLQI assessment. The mean Patient GA Psoriasis score at baseline was 4.0 and declined to 3.3 at 2 weeks and 1.7 at 24 weeks. This represented a mean improvement of 2.2 (95% CI, 2.2−2.3) at 24 weeks and a mean percentage improvement from baseline of 54%. In the Patient Itching Scale, the baseline score was 3.6 but improved to 2.9 at 2 weeks and 1.5 at 24 weeks, which constituted a mean improvement of 2.1 (95% CI, 2.0−2.2) at 24 weeks and a mean percentage improvement from baseline of 53%.

For joint-related characteristics, the percentage improvement from baseline in the HAQ DI was similar to improvements observed for the skin-related PRO measures (Figure). Mean HAQ DI scores improved from 0.79 at baseline to 0.63 at 2 weeks and 0.38 at 24 weeks. The mean improvement from baseline at 24 weeks was 0.41 (95% CI, 0.38–0.44). At 12 weeks, 47% of subjects achieved an MCID in the HAQ DI, and 41% of subjects achieved a HAQ DI score of 0. At 24 weeks, 52% of subjects achieved an MCID in the HAQ DI, and 47% of subjects achieved a HAQ DI score of 0.

Consistent with improvements in the total HAQ DI score, all subscales showed similar improvements during the 24-week course of therapy, with mean percentage improvement from baseline values ranging from 54% to 67%. The dressing and grooming subscale showed the highest mean percentage improvement from baseline at 24 weeks (67%).

The Patient GA Joint Disease and Patient GA Joint Pain scores also improved from baseline to 24 weeks of the trial. The mean Patient GA Joint Disease baseline score was 2.8 and improved by 14% at 2 weeks and by 47% at 24 weeks. Similarly, the mean Patient GA Joint Pain baseline score was 4.6 and improved by 17% at 2 weeks and by 48% at 24 weeks.

Responders to etanercept therapy, defined as those who achieved an MCID in the DLQI, the HAQ DI, or both, were observed in 81.2% of subjects at 12 weeks and in 85.0% of subjects at 24 weeks. Furthermore, 75.9% were responders as measured by the DLQI at 24 weeks, and 52.3% were responders as measured by the HAQ DI at 24 weeks. Those subjects that responded only in the DLQI totaled 32.6% of EDUCATE subjects, while 9.1% of subjects responded only in the HAQ DI. Importantly,

43.3% of subjects at 24 weeks reported clinically meaningful improvements in both DLQI and HAQ DI.

Comment

Patients with PsA in community dermatology settings reported substantial improvements in both skin- and joint-related PROs during a 24-week course of etanercept therapy. The improvements in the PROs occurred as early as 2 weeks after initiation of etanercept therapy.

Although RCTs establish drug safety and efficacy, enrollees in such studies can be small in number and relatively homogenous demographically. Consequently, studies such as EDUCATE provide valuable complementary information to the RCTs. In general, PROs in the EDUCATE study complement clinical information and provide insights to how patients perceive their disease.

At study entry, the physician's global assessment of psoriasis indicated that approximately 80% of subjects had moderate to severe levels of psoriasis and a mean percentage of body surface area affected by psoriasis of almost 30%. These data suggest that many EDUCATE enrollees had visible body parts (eg, hands, face) affected by psoriasis. Additional findings from this study demonstrate an additional reduction in health-related quality of life and mental health of the patient when visible body parts are affected.

In addition to skin-related manifestations, EDUCATE subjects also had joint disease at baseline as indicated by mean tender/painful joint count (approximately 10 joints) and mean swollen joint count (approximately 6 joints). Furthermore, a large proportion of subjects reported a history of sacroiliitis or spondylitis. The baseline values for the Patient GA Joint Disease and Patient GA Joint Pain also are indicative of considerable joint disease. The HAQ DI baseline value of 0.79 (Figure) suggests an important associated disability. The course of PsA joint disease, if untreated, can be highly negative. Kane et al[13] found that 47% of patients with PsA experienced joint erosion after a median of 2 years, but only 27% of patients had erosions at baseline. In another study, Harrison et al[14] determined that nearly a quarter of patients with PsA exhibit joint erosions one year after diagnosis. Taken together, these data suggest that untreated individuals with PsA can expect not only many disturbances in their activities of daily living but also a likelihood of permanent joint damage.

EDUCATE PROs data extend the findings of previous RCTs to the clinic.[4,5] In 2000, Mease et al[5] reported that the median improvement of scores on the Psoriasis Area and Severity Index was 46% after 12 weeks of etanercept therapy. In 2004, Mease et al[5] reported that the mean improvement from baseline scores in the Psoriasis Area and Severity Index was 42% after 24 weeks of etanercept therapy. Here, the mean improvement from baseline in the DLQI was 66% after 24 weeks. These data reflect a consistent pattern of clinically meaningful improvement in skin manifestations of PsA following etanercept treatment.

Previous PsA trials also captured data from the HAQ DI assessment. In 2004, Mease et al[4] reported a 54% mean improvement from baseline, which compares with a 57% mean improvement from baseline in EDUCATE. These HAQ improvements are similar to those reported in an earlier PsA trial.[5] Data from these 3 clinical trials strongly suggest that the extent and pace of symptom reduction in both the skin- and joint-related domains are consistent and reliable for patients with PsA receiving etanercept treatment.

We noted a striking distribution in clinical benefits for subjects with PsA. At 24 weeks, nearly half of the subjects improved as measured by both the DLQI and HAQ DI, while only a minority (15%) had no response. Interestingly, about one third of subjects only had a response in the DLQI and approximately 10% of subjects only had a response in the HAQ DI, suggesting the heterogeneous nature of PsA signs and symptoms.

Practicing dermatologists are increasingly aware that psoriasis can be associated with symptoms of arthritis.[15] In normal clinical practice, patients with skin-related symptoms may not complain about joint-related symptoms unless asked. Thus, dermatologists alert to the possibility of PsA may be able to uncover untreated cases of PsA if they query patients with evident psoriasis about joint symptoms. The results of the EDUCATE study show that etanercept treatment can confer benefits to the diverse population of patients with PsA found in a general dermatology practice, including those who were unaware that their skin- and joint-related symptoms had a common etiology.

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