ORIGINAL ARTICLE

Etanercept as Monotherapy in Patients with Psoriasis

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ABSTRACT

BACKGROUND

Inflammatory cytokines such as tumor necrosis factor (TNF) have been implicated in the pathogenesis of psoriasis. We evaluated the safety and efficacy of etanercept, a TNF antagonist, for the treatment of plaque psoriasis.

METHODS

In this 24-week, double-blind study, 672 patients underwent randomization and 652 either received placebo or received etanercept subcutaneously at a low dose (25 mg once weekly), a medium dose (25 mg twice weekly), or a high dose (50 mg twice weekly). After 12 weeks, patients in the placebo group began twice-weekly treatment with 25 mg of etanercept. The primary measure of clinical response was the psoriasis area-and-severity index.

RESULTS

At week 12, there was an improvement from base line of 75 percent or more in the psoriasis area-and-severity index in 4 percent of the patients in the placebo group, as compared with 14 percent of those in the low-dose–etanercept group, 34 percent in the medium-dose–etanercept group, and 49 percent in the high-dose–etanercept group ($P<0.001$ for all three comparisons with the placebo group). The clinical responses continued to improve with longer treatment. At week 24, there was at least a 75 percent improvement in the psoriasis area-and-severity index in 25 percent of the patients in the low-dose group, 44 percent of those in the medium-dose group, and 59 percent in the high-dose group. The responses as measured by improvements in the psoriasis area-and-severity index were paralleled by improvements in global assessments by physicians and the patients and in quality-of-life measures. Etanercept was generally well tolerated.

CONCLUSIONS

The treatment of psoriasis with etanercept led to a significant reduction in the severity of disease over a period of 24 weeks.

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Psoriasis is a chronic inflammatory skin disorder that affects approximately 2 percent of the world's population.[1] Patients report substantial disease-related inability to work[2] and may face discrimination, financial distress, or depression.[3] Rapp et al.[4] showed that psoriasis causes more physical and mental disability than many major diseases. Current therapies for psoriasis are not satisfactory.[3] Many therapies are associated with cumulative toxicity that may limit their usefulness in this chronic disease.[1-4]

Psoriasis is characterized by the infiltration of the skin by activated T cells and an abnormal proliferation of keratinocytes. As a result of overproduction by T cells, keratinocytes, dendritic cells, and Langerhan's cells, the concentrations of the inflammatory cytokine tumor necrosis factor (TNF) are higher in psoriatic lesions than in uninvolved skin in patients with psoriasis or in normal persons.[5-8] Serum and lesional TNF concentrations decrease after the effective treatment of psoriasis, and these decreases correlate with clinical improvement, suggesting that TNF has an important role in the disease.[9] Recognition of the contributions of T cells and inflammatory cytokines to the pathogenesis of psoriasis has led to the development of new biologic treatment strategies.

Etanercept is a recombinant human TNF-receptor fusion protein that antagonizes the effects of endogenous TNF by competitively inhibiting its interaction with cell-surface receptors. Etanercept has been shown to be effective in patients with rheumatoid arthritis[10,11] and in patients with psoriatic arthritis, in whom etanercept also improved psoriatic skin lesions.[12,13] On the basis of these results, we conducted a study to evaluate the safety and efficacy of three different regimens of etanercept in patients with moderate-to-severe psoriasis.

METHODS

STUDY PATIENTS

The institutional review boards of the participating medical centers approved the protocol, and all patients gave written informed consent before any study-related procedures were performed. Patients were eligible if they were at least 18 years of age, had active but clinically stable plaque psoriasis involving at least 10 percent of the body-surface area, had a minimal psoriasis area-and-severity index[14] of 10 (indicating moderate-to-severe psoriasis) during the screening period, and had previously received phototherapy or systemic psoriasis therapy at least once or had been a candidate for such therapy. Patients with guttate, erythrodermic, or pustular psoriasis at the time of screening were excluded, as were those with other active skin conditions that would interfere with evaluations. Patients were also excluded if they had previously received etanercept or antibody to TNF; if they had received anti-CD4 antibodies or interleukin-2–diphtheria-toxin fusion protein within the previous six months; if they had received any biologic or investigational drug, psoralen–ultraviolet A phototherapy, systemic corticosteroids, or systemic psoriasis therapy within the previous four weeks; if they had received ultraviolet B phototherapy, topical corticosteroids, vitamin A or D analogues, or anthralin within the previous two weeks; or if they had taken antibiotics within the previous week. Patients were permitted to use stable doses of topical corticosteroids on the scalp, axilla, and groin during the study if these preparations were of low or moderate potency.

STUDY DRUG

Etanercept (Enbrel, Immunex–Wyeth) was supplied to patients in syringes, each containing the contents of one reconstituted vial of etanercept or matching placebo. All study drug was administered by the patient by subcutaneous injection.

STUDY DESIGN

This was a placebo-controlled, double-blind, parallel-group, phase 3 study that evaluated etanercept as a treatment for psoriasis in patients at 47 sites in the United States. Eligible patients were randomly assigned to receive placebo or etanercept for 24 weeks. During the first 12 weeks of the double-blind treatment period, patients received etanercept at a low dose (25 mg once weekly), a medium dose (25 mg twice weekly), or a high dose (50 mg twice weekly) or placebo. In order to maintain masking with respect to the treatment assignments, all patients received two injections per dose of study drug, with placebo making up the balance of injections for patients assigned to the low-dose–etanercept regimen or the medium-dose–etanercept regimen. After 12 weeks of treatment, patients in the placebo group began double-blind treatment with etanercept (at the medium dose, 25 mg twice weekly). Safety and efficacy were evaluated at weeks 2, 4, 8, 12, 16, 20, and 24. The first patient underwent randomization in December 2001, and the last patient in April 2002; the week 24 observation was made in

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the last patient in October 2002. Patients underwent central randomization with the use of a permuted-block randomization list, with equal allocation to each of the four treatment groups.

The study was designed by Immunex, Dr. Gottlieb, and other members of the Etanercept Psoriasis Study Group. Data were collected by the investigators in the study group (the complete data set was held at the central data-processing facility at Amgen) and were analyzed by Dr. Zitnik and Ms. Wang. The academic investigators had full access to the data. The lead investigators wrote the paper with editorial assistance from Amgen and Immunex, and the investigators made the decisions about publication in collaboration with Amgen.

EFFICACY END POINTS

The primary measure of efficacy was the proportion of patients in each treatment group in whom there was an improvement of at least 75 percent from base line in the psoriasis area-and-severity index at week 12. The index was calculated according to the standard method outlined by Fredriksson and Pettersson.[14] The psoriatic lesions are scored on a scale of 0 to 4 for three characteristics: erythema, induration, and desquamation. The lesions are scored within four anatomical regions: head, trunk, arms, and legs. Within each of these regions, the area of involvement is scored on a scale of 0 to 6. Each region's contribution to the overall body-surface area is corrected for by a separate coefficient. The corrected scores for each region are summed to provide the overall index. The index ranges from 0 (no psoriasis) to 72 (severe disease). The proportions of patients with an improvement in the index of at least 50 percent and the proportions with an improvement of at least 90 percent were also determined. The Physician's Static Global Assessment of Psoriasis was reported on a scale of 0 to 5, with 0 indicating no psoriasis (clear of disease) and higher scores indicating more severe disease. Two patient-reported outcomes were assessed: the Dermatology Life Quality Index, calculated from a summary of 10 items on a patient questionnaire in which all the items were weighted equally, which has been validated for use in patients with psoriasis,[15] and the Patient's Global Assessment of Psoriasis (on a scale ranging from 0 [good] to 5 [severe]).

SAFETY END POINTS

All patients who underwent randomization and received at least one dose of study drug were included in the safety analysis, including analysis of adverse events, infections, and premature withdrawal from the study. Standard laboratory tests, including hematologic analysis, analysis of serum chemistry, and urinalysis profiles were performed at screening, at base line, and at weeks 12 and 24. Adverse events and abnormal laboratory values were graded on a scale derived from the Common Toxicity Criteria of the National Cancer Institute. Serum samples obtained at base line and week 24 were tested for antibody to etanercept with the use of an enzyme-linked immunosorbent assay (ELISA).[16] Samples that were positive on ELISA were tested for neutralizing antibodies with the use of a binding assay.

STATISTICAL ANALYSIS

All patients who received at least one dose of double-blind study treatment were included in the analyses. All statistical tests were two-sided with a significance (α) level of 0.05. Comparisons between treatment groups were made with the use of Pearson's chi-square test or Fisher's exact test for binary end points, the Mantel–Haenszel row mean score test for ordinal end points, and nonparametric tests (such as the Wilcoxon rank-sum test) for continuous end points. The last observations were carried forward in cases of missing data or early termination.

The primary efficacy analysis compared each of the three etanercept groups with the placebo group in terms of the proportion of patients with an improvement of at least 75 percent in the psoriasis area-and-severity index at week 12. Comparisons were made with the use of Pearson's chi-square test. Hochberg's step-up procedure for multiple comparisons was used to maintain the significance level at 0.05 for the three comparisons. Statistical comparisons at time points other than 12 weeks were not corrected for multiple comparisons.

The primary analysis was performed after all patients completed the week 12 assessments. All patients and study-site personnel, however, remained unaware of the results and the treatment-group assignments. Additional analyses of the data from the 24 weeks of double-blind treatment were performed after all patients completed the week 24 assessment.

The sample size was chosen both to test the efficacy of etanercept and to expose an adequate number of patients to treatment for the assessment of safety. The sample size was estimated for the primary efficacy measurement. On the basis of the results observed in a phase 2 study, this study had more than 99 percent power to detect a difference

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of 25 percent in the proportion of patients with an improvement of at least 75 percent in the psoriasis area-and-severity index between an etanercept group and the placebo group. The primary analysis was performed after week 12, and no interim analyses were performed.

RESULTS

STUDY PATIENTS

A total of 672 patients underwent randomization, and 652 patients received at least one dose of double-blind study treatment. Twenty patients were randomly assigned to a treatment group but did not receive any study drug (two patients in the placebo group, nine in the low-dose–etanercept group, five in the medium-dose–etanercept group, and four in the high-dose–etanercept group). The primary analyses of efficacy and safety are based on the 652 patients who received at least one dose. The groups were balanced in terms of demographic characteristics, disease history, and the severity of disease at base line (Table 1). The population of patients in this study was predominantly male (67 percent) and white (87 percent), and the mean age was 45.1 years. The mean duration of psoriasis was 18.7 years, and 22 percent of the patients had psoriatic arthritis. Eighty-eight percent of patients had previously received topical corticosteroids, and 76 percent had previously received systemic therapy or phototherapy for psoriasis. The mean affected body-surface area was 28.7 percent, and the mean base-line psoriasis area-and-severity index was 18.4. Overall, 94 percent of the patients completed 12 weeks of treatment and 88 percent completed 24 weeks, with similar proportions of patients completing treatment in each group.

EFFICACY

The primary efficacy end point for this study was the proportion of patients with an improvement of at least 75 percent in the psoriasis area-and-severity index at week 12 (Table 2). At week 12, there was such an improvement in 4 percent of the patients

Table 1. Base-Line Demographic and Clinical Characteristics of the Patients.*

Characteristic	Placebo Group (N=166)	Etanercept Groups		
		Low-Dose (N=160)	Medium-Dose (N=162)	High-Dose (N=164)
Age (yr)	45.6±1.0	44.4±0.9	45.4±1.0	44.8±0.8
Age ≥65 yr (%)	7	5	9	4
Male sex (%)	63	74	67	65
White race (%)	90	85	85	87
Duration of psoriasis (yr)	18.4±0.9	19.3±0.9	18.5±0.9	18.6±0.9
Affected body-surface area (%)	28.8±1.4	27.7±1.5	28.5±1.6	29.9±1.6
Psoriasis area-and-severity index†	18.3±0.6	18.2±0.7	18.5±0.7	18.4±0.7
Patients assessed by the physician as having marked or severe psoriasis (%)‡	23	21	23	21
Patients with self-assessed high severity (%)§	75	76	74	76
Dermatology Life Quality Index¶	12.8±0.6	12.2±0.5	12.7±0.5	11.3±0.5

* Plus–minus values are means ±SE.

† The psoriasis area-and-severity index ranges from 0 to 72, with 0 indicating no psoriasis and 72 indicating severe disease. The index is calculated according to the following formula:

$$0.1\,(E_h+I_h+D_h)\,A_h+0.3\,(E_t+I_t+D_t)\,A_t+0.2\,(E_u+I_u+D_u)\,A_u+0.4\,(E_l+I_l+D_l)\,A_l,$$

where A represents the area of psoriatic involvement (on a scale of 0 to 6), E represents the severity of psoriatic lesions in terms of erythema (on a scale of 0 to 4), I represents the severity of psoriatic lesions in terms of infiltration (on a scale of 0 to 4), D represents the severity of psoriatic lesions in terms of desquamation (on a scale of 0 to 4), and h denotes the head, t the trunk, u the upper extremities, and l the lower extremities.

‡ Data are for patients with a base-line score of 4 (marked) or 5 (severe) on the Physician's Static Global Assessment; scores range from 0 to 5, with 0 indicating no evidence of plaque elevation, erythema, or scaling and 5 indicating severe induration, erythema, and scaling.

§ Data are for patients with a psoriasis score of 4 or 5 on the Patient's Global Assessment of Psoriasis; scores range from 0 to 5, with 0 indicating good and 5 indicating severe.

¶ The Dermatology Life Quality Index ranges from 0 to 30, with 0 indicating best and 30 indicating worst.

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in the placebo group, as compared with 14 percent in the low-dose–etanercept group, 34 percent in the medium-dose–etanercept group, and 49 percent in the high-dose–etanercept group (P<0.001 for all three comparisons with the placebo group). There was a statistically significant difference from the placebo group in the proportion of patients with such an improvement as early as week 4 in the high-dose group and week 8 in the medium-dose group.

The proportion of patients with an improvement in the psoriasis area-and-severity index of at least 50 percent in all three etanercept groups and the proportion with an improvement of at least 90 percent in the medium-dose and high-dose groups were also significantly different from the proportions in the placebo group at week 12 (Table 2). The mean percentage improvements in the psoriasis area-and-severity index from base line were statistically significant for all three etanercept groups as early as week 2 of the study; by week 12, the mean level of improvement was 40.9 percent in the low-dose group, 52.6 percent in the medium-dose group, and 64.2 percent in the high-dose group, as compared with 14.0 percent in the placebo group (Table 2 and Fig. 1).

Results of the week 24 evaluations are also presented in Table 2. At week 24, an improvement of 75 percent or more had been achieved in 25 percent

Table 2. Clinical Responses at Week 12 and Week 24.*

End Point	Week 12				Week 24		
	Placebo Group (N=166)	Low-Dose–Etanercept Group (N=160)	Medium-Dose–Etanercept Group (N=162)	High-Dose–Etanercept Group (N=164)	Low-Dose–Etanercept Group (N=160)	Medium-Dose–Etanercept Group (N=162)	High-Dose–Etanercept Group (N=164)
End points reported by the physician or dermatologist							
Level of improvement in the PASI — no. of patients (%)							
≥50%	24 (14)	65 (41)†	94 (58)†	121 (74)†	92 (58)	113 (70)	127 (77)
≥75%‡	6 (4)	23 (14)†	55 (34)†	81 (49)†	40 (25)	71 (44)	97 (59)
≥90%	1 (1)	5 (3)	19 (12)†	36 (22)†	9 (6)	32 (20)	49 (30)
Percentage improvement in PASI	14.0±2.6	40.9±2.4†	52.6±2.7†	64.2±2.4†	50.3±2.5	62.1±2.5	71.1±2.2
PASI§							
Median	14.4	9.6	6.5	4.2	7.0	4.8	3.0
Range	1.6–49.1	0.7–70.8	0.0–51.9	0.0–48.0	0.0–54.0	0.0–29.4	0.0–48.0
"Clear" or "almost clear" status — no. of patients (%)	8 (5)	37 (23)†	55 (34)†	81 (49)†	41 (26)	63 (39)	90 (55)
End points reported by the patient							
Percentage improvement in Dermatology Life Quality Index	10.9±4.8	47.2±2.9†	50.8±3.8†	61.0±4.3†	54.0±3.0	59.4±3.6	73.8±2.8
Patient's global assessment of psoriasis — no. of patients (%)¶							
0 (Good)	0	3 (2)	18 (11)	32 (20)	11 (7)	29 (18)	55 (34)
1	9 (5)	24 (15)	39 (24)	50 (30)	39 (24)	46 (28)	53 (32)
2	24 (14)	34 (21)	39 (24)	38 (23)	43 (27)	28 (17)	23 (14)
3	41 (25)	56 (35)	34 (21)	23 (14)	35 (22)	35 (22)	22 (13)
4	52 (31)	27 (17)	17 (10)	15 (9)	23 (14)	18 (11)	9 (5)
5 (Severe)	40 (24)	16 (10)	15 (9)	6 (4)	9 (6)	6 (4)	2 (1)

* Plus–minus values are means ±SE. A last-observation-carried-forward approach was used for patients with missing data or early termination. Two-tailed P values were calculated with the use of the Pearson's chi-square test for binary end points, the Mantel–Haenszel row mean scores test for ordinal end points, and the Wilcoxon rank-sum test for continuous end points. PASI denotes psoriasis area-and-severity index.
† P<0.001 for the comparison with the placebo group at week 12.
‡ An improvement of at least 75 percent at week 12 was the primary efficacy end point.
§ The index ranges from 0 to 72, with 0 indicating no psoriasis and 72 indicating maximally severe disease.
¶ P<0.001 for all comparisons with the placebo group at week 12.

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of the patients in the low-dose–etanercept group, 44 percent of those in the medium-dose group, and 59 percent of those in the high-dose group. Because the patients in the placebo group received etanercept after week 12, this analysis did not include a placebo control. At week 24, an improvement of 75 percent or more had been achieved in 33 percent of the patients in the original placebo group who had begun receiving etanercept after week 12 — a response rate that is consistent with that in the medium-dose–etanercept group at week 12 (34 percent) (Table 2).

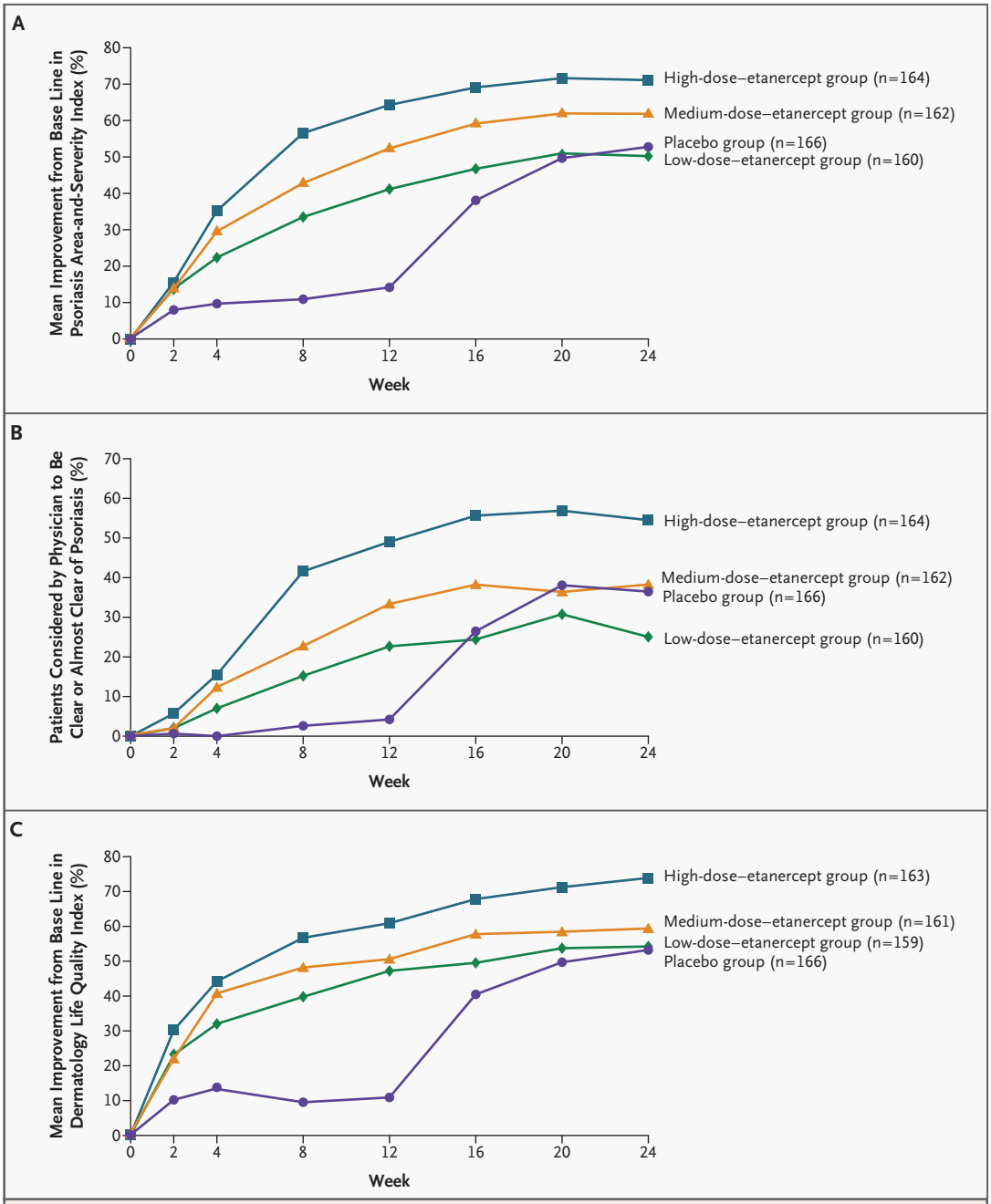

Figure 1. Clinical Response to Etanercept Treatment as Measured by the Psoriasis Area-and-Severity Index (Panel A), the Physician's Static Global Assessment (Panel B), and the Patient-Reported Dermatology Life Quality Index (Panel C).
After week 12, patients in the original placebo group were treated with etanercept.

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At week 12, the proportion of patients in each of the etanercept groups who were assessed by the physician as being clear or almost clear of psoriasis was significantly different from that in the placebo group (P<0.001 for all three comparisons) (Table 2). These differences were significant for all the etanercept groups as early as week 4 of the study. In addition, at week 2, the Physician's Static Global Assessment in all the etanercept groups was significantly different from that in the placebo group.

The mean percentage improvement from base line in the Dermatology Life Quality Index was significant in all the etanercept groups at week 2; by week 12, the mean improvement was 47.2 percent in the low-dose group, 50.8 percent in the medium-dose group, and 61.0 percent in the high-dose group, as compared with 10.9 percent in the placebo group (P<0.001 for all three comparisons with the placebo group) (Fig. 1). Scores on the Patient's Global Assessment in all three etanercept groups were also significantly different from those in the placebo group at week 12 (P<0.001 for all comparisons) (Table 2). As early as week 2, the global assessments by the patients in all the etanercept groups were significantly different from those in the placebo group.

SAFETY

Etanercept was well tolerated in this population of patients, with adverse events and infections occurring in similar proportions of patients in each group during the study (Table 3). Most events were of mild or moderate intensity. During the 24-week study, 27 patients withdrew because of adverse events, and 16 withdrew because of lack of efficacy. No cases of tuberculosis or opportunistic infections were reported during the study.

All laboratory abnormalities were of mild or moderate intensity, and no patient withdrew because of an abnormal laboratory result. Eight etanercept-treated patients had serum samples that tested positive for non-neutralizing anti-etanercept antibodies, as determined by ELISA and a binding assay. We did not observe differences in efficacy or adverse-event profiles between these eight patients and the patients without anti-etanercept antibodies, but the small number provided limited statistical power.

DISCUSSION

Our large, multicenter trial demonstrates the efficacy and tolerability of etanercept, a TNF antagonist, in the treatment of psoriasis. The study underscores the critical role of TNF in the pathogenesis of this debilitating disease.

In this study, etanercept was effective in patients with psoriasis. Significant, dose-dependent increases were observed at the 12-week assessment in the proportions of patients in whom an improvement of at least 75 percent in the psoriasis area-and-severity index was achieved, and improvement con-

Table 3. Adverse Events Occurring in at Least 5 Percent of Patients in Any Treatment Group.

Type of Event	All Treatment Groups at Wk 12				Placebo Group		Etanercept Groups, Base Line to Wk 24		
	Placebo Group (N=166)	Low-Dose–Etanercept Group (N=160)	Medium-Dose–Etanercept Group (N=162)	High-Dose–Etanercept Group (N=164)	Base Line to Wk 12 (Placebo) (N=166)	Wk 12 to Wk 24 (Medium-Dose Etanercept) (N=153)	Low-Dose (N=160)	Medium-Dose (N=162)	High-Dose (N=164)
	number of patients (percent)								
Injection-site reaction	12 (7)	17 (11)	28 (17)	22 (13)	12 (7)	10 (7)	22 (14)	33 (20)	26 (16)
Headache	11 (7)	5 (3)	19 (12)	11 (7)	11 (7)	8 (5)	8 (5)	20 (12)	14 (9)
Upper respiratory infection	19 (11)	16 (10)	15 (9)	9 (5)	19 (11)	9 (6)	22 (14)	23 (14)	20 (12)
Injection-site ecchymosis	6 (4)	11 (7)	4 (2)	8 (5)	6 (4)	3 (2)	11 (7)	5 (3)	8 (5)
Asthenia	5 (3)	7 (4)	6 (4)	3 (2)	5 (3)	2 (1)	9 (6)	12 (7)	5 (3)
Myalgia	4 (2)	3 (2)	6 (4)	3 (2)	4 (2)	3 (2)	8 (5)	12 (7)	7 (4)
Accidental injury	7 (4)	6 (4)	5 (3)	7 (4)	7 (4)	6 (4)	11 (7)	11 (7)	11 (7)
Sinusitus	1 (1)	0	0	0	1 (1)	2 (1)	9 (6)	10 (6)	8 (5)
Nausea	2 (1)	5 (3)	4 (2)	3 (2)	2 (1)	1 (1)	8 (5)	5 (3)	5 (3)
Rash	4 (2)	4 (3)	4 (2)	5 (3)	4 (2)	0	4 (2)	6 (4)	10 (6)

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tinued with continued etanercept therapy. The mean percentage improvements from base line in the response as measured by this index were statistically significant in the three etanercept groups as early as week 2.

Etanercept induced a marked clearance of psoriatic skin lesions. A significantly greater proportion of etanercept-treated patients than patients in the placebo group had a "clear" or "almost clear" status at the 12-week assessment, and the responses continued to improve in a dose-dependent manner through 24 weeks of treatment.

The evaluation of the treatment effect in psoriasis solely with the use of physician-reported end points that rely mainly on the body-surface area involved may be suboptimal. The patient's perspective on the improvement of skin disease and the quality of life should also be considered.[17] In addition, rapid clearing of skin lesions is an important aspect of effective psoriasis management and may correlate with the patient's satisfaction with treatment.[3] After two weeks of treatment, etanercept produced statistically significant and clinically meaningful improvements in patients' global assessments of disease and in the quality of life as assessed by the Dermatology Life Quality Index.

Etanercept was well tolerated in this study. The proportions of patients with adverse events and infections were similar in all active-treatment groups and the placebo group at week 12. We could not compare the etanercept groups with the placebo group with respect to safety at week 24 because of the crossover of patients from placebo to active drug at week 12. The pattern of infections and adverse events, however, did not change through 24 weeks of therapy. The dose of 50 mg of etanercept administered twice weekly that was used in the high-dose group in this study was higher than that used in previous studies of rheumatoid arthritis and psoriatic arthritis.[10,13] In this study, the safety profile was similar to that observed in the group receiving 25 mg of etanercept twice weekly. Given the apparent increase in efficacy achieved with the higher dose, the risk–benefit ratio is favorable.

Our results are interesting in the light of increasing clinical evidence that the disruption of specific immune interactions can improve psoriasis. Other agents being evaluated for the treatment of psoriasis include another TNF antagonist, infliximab,[18,19] an anti-CD11a monoclonal antibody, efalizumab,[20] and a soluble LFA-3–IgG fusion protein, alefacept.[21] The efficacy results of our study underscore the importance of TNF and its inhibition in psoriasis.

TNF and interferon-γ are produced by type 1 helper T cells (Th1) found in psoriatic plaques.[22] TNF induces the expression of adhesion molecules such as intercellular adhesion molecule 1 and vascular-cell adhesion molecule on keratinocytes and vascular endothelial cells and induces the production of chemokines including interleukin-8. The production of adhesion molecules and chemokines results in the recruitment of additional inflammatory cells to the plaque. The recruited cells can then produce further TNF and interferon-γ, potentially amplifying local inflammation and keratinocyte proliferation.[22] By inhibiting the activity of TNF, etanercept may block this cycle of inflammation, rapidly improving skin lesions. This effect is evidenced by recent observations showing that treatment with TNF antagonists results in a reduction in epidermal T-cell infiltration.[19,23] In acting through a recruitment pathway, TNF antagonists reduce epidermal T-cell infiltration without causing T-cell depletion.

Etanercept has been approved for use in adults with rheumatoid arthritis since 1998 and for children with juvenile rheumatoid arthritis since 1999. Long-term clinical safety studies in more than 2000 patients and post-marketing experience in more than 150,000 patients have shown the continued efficacy and favorable risk–benefit profile of etanercept.[24] Although data regarding long-term safety in patients with psoriasis are not available, the data from patients with rheumatoid arthritis suggest that long-term treatment with etanercept may be a viable option for patients with psoriasis — an important consideration in the management of this chronic disease.

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Drs. Leonardi, Powers, Goffe, and Gottlieb report having served as consultants for Amgen, and Drs. Leonardi, Goffe, and Gottlieb report having served as paid lecturers for Amgen. Dr. Gottlieb reports having served as a consultant and paid lecturer for Johnson & Johnson, Genentech, and Biogen; Dr. Leonardi reports having served as a consultant and paid lecturer for Johnson & Johnson and Genentech; Dr. Powers reports having served as a consultant for Genentech and Biogen; and Dr. Goffe reports having served as a consultant and paid lecturer for Biogen. Dr. Zitnik and Ms. Wang report owning equity in Amgen.

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APPENDIX

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