Long-term etanercept in pediatric patients with plaque psoriasis

Amy S. Paller, MD,[a] Elaine C. Siegfried, MD,[b] Lawrence F. Eichenfield, MD,[c] David Pariser, MD,[d] Richard G. Langley, MD,[e] Kara Creamer, MS,[f] and Greg Kricorian, MD[f]

Chicago, Illinois; Saint Louis, Missouri; San Diego and Thousand Oaks, California; Norfolk, Virginia; and Halifax, Nova Scotia, Canada

Background: No systemic therapies are approved by the US Food and Drug Administration for the treatment of psoriasis in children and adolescents.

Objective: We sought to evaluate the long-term safety and efficacy of etanercept in pediatric patients (aged 4-17 years) with moderate to severe plaque psoriasis.

Methods: Patients who completed or received substantial treatment benefit in a 48-week, randomized, double-blind, placebo-controlled study (N = 211) evaluating the efficacy and safety of once-weekly etanercept (0.8 mg/kg) were enrolled in this 264-week open-label extension study. The primary end point was the occurrence of adverse events. Secondary end points included Psoriasis Area and Severity Index 50%, 75%, and 90% responses compared with baseline; static Physician Global Assessment; and clear and clear/almost clear static Physician Global Assessment status. Results from a 96-week interim analysis are presented.

Results: Of 182 enrolled patients, 181 received treatment and 140 (76.9%) completed week 96. A total of 145 patients (80.1%) reported adverse events; 5 serious adverse events occurred in 3 patients, none of which were treatment related. Observed Psoriasis Area and Severity Index 50% (89%), 75% (61%), and 90% (30%) responses compared with baseline at week 96 were similar to those observed in the double-blind trial. The static Physician Global Assessment was maintained through week 96, when 47% of patients achieved clear/almost clear status.

Limitations: This is an interim analysis from an open-label study.

Conclusion: Extended treatment with etanercept in pediatric patients with moderate to severe plaque psoriasis was generally well tolerated, and efficacy was maintained through 96 weeks. (J Am Acad Dermatol 2010;63:762-8.)

Key words: efficacy; etanercept; long-term treatment; pediatric patients; plaque psoriasis; safety.

From the Children's Memorial Hospital and Northwestern University Medical School, Chicago[a]; Cardinal Glennon Children's Hospital and Saint Louis University[b]; Rady Children's Hospital and University of California, San Diego[c]; Eastern Virginia Medical School and Virginia Clinical Research[d]; Division of Dermatology, Dalhousie University, Halifax[e]; and Amgen Inc, Thousand Oaks.[f]

Supported by Immunex Corp, a wholly owned subsidiary of Amgen Inc, and by Wyeth, which was acquired by Pfizer Inc in October 2009.

Disclosure: Dr Paller has served as an investigator for Amgen without compensation but has received honoraria from Abbott and Centocor as a consultant. Dr Siegfried has served as an investigator for Amgen without compensation but has received honoraria from Abbott and Amgen as a consultant. Dr Eichenfield has served as an investigator for Amgen without compensation but has received honoraria from Amgen and Centocor/Johnson & Johnson as a consultant. Dr Pariser has received investigator grants from Amgen, Abbott, Centocor, Novartis, and Pfizer and has received honoraria for serving on scientific advisory boards for Amgen and Centocor and as a speaker for Wyeth. Dr Langley has received investigator grants from Abbott, Amgen, Biogen Idec, Centocor, LEO Pharma, Celgene, Ortho Biotec, Pfizer, and Wyeth and has received honoraria for serving on the scientific advisory boards for Abbott, Amgen, Centocor, Ortho Biotec, and Wyeth and as a speaker for Abbott, Amgen, Centocor, Ortho Biotec, and Wyeth. Ms Creamer and Dr Kricorian are Amgen employees and have Amgen stock and stock options.

This study is registered with ClinicalTrials.gov with the identifier NCT00078819.

Accepted for publication April 2, 2010.

Reprint requests: Amy S. Paller, MD, Department of Dermatology, Northwestern University Medical School, 676 N Saint Clair St, Suite 1600, Chicago, IL 60611-2997. E-mail: apaller@northwestern.edu.

Published online June 4, 2010.

0190-9622/$36.00

doi:10.1016/j.jaad.2010.04.004

Etanercept is indicated for use in adults with chronic moderate to severe plaque psoriasis and in patients aged 2 years or older for treatment of moderately to severely active polyarticular juvenile idiopathic arthritis and other indications.[1] Previously, etanercept has been shown to be generally well tolerated and to provide patient benefit, with significant reductions in disease severity in adults with psoriasis.[2-5]

We previously assessed etanercept treatment in children and adolescents with moderate to severe plaque psoriasis (study 20030211).[6] Patients receiving etanercept had statistically and clinically significant reductions in disease severity beginning as early as week 4 that were maintained throughout the study. Treatment was well tolerated, but the trial was of relatively short duration (48 weeks), and a long-term observation of etanercept treatment is necessary to further assess its safety profile in this patient population. The current extension study was designed to evaluate long-term treatment with etanercept in pediatric patients with moderate to severe plaque psoriasis who had participated in study 20030211.

CAPSULE SUMMARY

- Etanercept treatment was assessed in pediatric patients with plaque psoriasis in a 96-week open-label extension of a previously reported 48-week randomized, double-blind trial.
- Etanercept was generally well tolerated in the time period studied.
- Treatment efficacy was maintained during the open-label extension period.

METHODS

Patients

Patients aged 4 to 17 years with moderate to severe plaque psoriasis were eligible if they completed study 20030211 or received substantial benefit from etanercept on or after week 12 with no serious adverse event (SAE) or other clinically significant adverse event (AE) considered related to study drug. Substantial benefit was defined as achievement of a minimum Psoriasis Area and Severity Index (PASI) 50% response compared with baseline (PASI 50) of study 20030211.

Study design

This was an open-label, multicenter, extension trial evaluating long-term treatment with once-weekly etanercept at 0.8 mg/kg (maximum 50 mg) in pediatric patients with moderate to severe plaque psoriasis for a planned duration of 264 weeks after completion of study 20030211. Patients were allowed to use topical standard-of-care therapy, including mild- to moderate-potency topical corticosteroids, during the study. The study was conducted at 37 sites in the United States and Canada. Results from a 96-week interim analysis of the extension study are presented here (ie, 144 weeks total). This analysis includes data available as of November 18, 2008.

The study was conducted in accordance with International Conference on Harmonization Good Clinical Practice regulations and guidelines. The institutional review boards of the participating medical centers approved the protocol and amendments. Written informed consent was obtained from the parents or legal guardians of all patients, and assent was obtained from all appropriate patients as requested by the institutional review boards.

End points/assessments

The primary end point was the occurrence of AEs, including infectious episodes, SAEs, and serious infectious episodes. Secondary efficacy end points included PASI 50, PASI 75% response compared with baseline (PASI 75), and PASI 90% response compared with baseline (PASI 90); percentage improvement in PASI score and Children's Dermatology Life Quality Index (CDLQI); improvement in joint pain; static Physician Global Assessment (sPGA); and clear and clear/almost clear sPGA status (score of 0 or 1). Two versions of the CDLQI questionnaire were used. Patients aged 4 to 7 years were administered a cartoon version to be completed with parent/caregiver help, and those aged 8 to 12 years completed the cartoon version themselves. Patients aged 13 to 17 years completed a text version. Joint pain was assessed using a 10-point scale in which 0 represents no pain and 10 represents severe pain.

Secondary safety end points included measurements of injection site reactions; exposure-adjusted event rates for AEs, infections, and injection site reactions; physical examination, including height and weight; vital signs; and AEs and laboratory toxicity graded according to the National Cancer Institute Common Toxicity Criteria (Version 2.0). An SAE was defined as one that resulted in death, was life threatening, required inpatient or prolonged hospitalization, resulted in persistent or significant disability or incapacity, or was a congenital anomaly or birth defect. Data pertaining to antinuclear antibody (ANA) formation are included in this interim analysis. Data pertaining to formation of anti-etanercept antibodies will not be assessed until the final analysis.