Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis

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Background: There are no systemic therapies approved in the United States to treat pediatric psoriasis.

Objective: We sought to evaluate long-term safety and efficacy of etanercept in children and adolescents with moderate to severe plaque psoriasis.

Methods: This 5-year, open-label extension study enrolled patients aged 4 to 17 years who had participated in a 48-week parent study. End points included occurrence of adverse events (AEs) and serious AEs including infections, and rates of 75% and 90% improvement in Psoriasis Area and Severity Index score and clear/almost clear on static physician global assessment.

Results: Of 182 patients enrolled, 181 received etanercept and 69 completed 264 weeks. Through week 264, 161 (89.0%) patients reported an AE, most commonly upper respiratory tract infection (37.6%), nasopharyngitis (26.0%), and headache (21.5%). Seven patients reported 8 serious AEs; only 1 (cellulitis) was considered treatment-related. No cases of opportunistic infections or malignancy were reported. Rates of 75% improvement in Psoriasis Area and Severity Index score (~60%–70%) and 90% improvement in Psoriasis Area and Severity Index score (~30%–40%) and static physician global assessment status clear/almost clear (~40%–50%) were maintained through week 264.

Limitations: The number of patients remaining on study at week 264 was small.

Conclusion: Etanercept in pediatric patients was generally well tolerated and efficacy was maintained in those who remained in the study for up to 264 weeks. (J Am Acad Dermatol 2016;74:280-7.)

Key words: etanercept; long-term safety; open-label; pediatric population; plaque psoriasis.

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The overall annual incidence of psoriasis in children and adolescents in the United States (from birth to 18 years of age) was estimated to be 41 cases per 100,000 person-years during the period from 1970 through 1999, and the annual incidence increased during that time.[1] Approximately one third of adult patients with psoriasis report the development of psoriasis symptoms before adulthood.[2,3] From 1979 through 2007, pediatric patients had approximately 3.8 million health care visits for their psoriasis, representing a considerable health care burden.[4] Comorbidities associated with pediatric psoriasis include metabolic syndrome, hypertension, hyperlipidemia, diabetes mellitus, rheumatoid arthritis, and Crohn's disease.[5,6] Pediatric patients have impaired health-related quality of life (HRQOL) from their psoriasis, particularly with respect to emotional and school functioning.[7,8] The cumulative life course impairment as a result of psoriasis, which affects the ability for individuals to fulfill their full lifetime potential, is particularly devastating for adolescents and young adults compared with patients who have adult-onset psoriasis.[9]

CAPSULE SUMMARY

- A 48-week etanercept study in patients with pediatric psoriasis demonstrated promising tolerability and efficacy.
- This open-label, 264-week extension study showed no unexpected adverse events and efficacy was maintained.
- Etanercept could be an option for pediatric psoriasis; access is limited by lack of disease-specific labeling.

Therapies currently approved by the US Food and Drug Administration (FDA) for the treatment of pediatric psoriasis in the United States include only a small number of topical agents with labeled indications limited to children 12 years of age or older. Of the interventions used for the treatment of moderate to severe plaque psoriasis in adults (phototherapy, methotrexate, cyclosporine, oral retinoids, or biologic agents) none is FDA-approved for children with moderate to severe psoriasis. Access to effective systemic treatments is limited for children and adolescents with psoriasis because of the lack of data and labeled indication.[10]

Etanercept is a soluble tumor necrosis factor receptor fusion protein that reversibly binds to tumor necrosis factor. Etanercept is approved for the treatment of adults with moderately to severely active rheumatoid arthritis, active psoriatic arthritis, active ankylosing spondylitis, and moderate to severe plaque psoriasis. Etanercept has also been approved since 1999 in the United States to treat children with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) down to 2 years of age.[11] Etanercept has been shown to be effective for the treatment of JIA at 0.8 mg/kg once weekly (maximum 50 mg) with a favorable safety profile during long-term therapy.[12,13] We now report 5-year results from an open-label extension (OLE) study to examine the safety and efficacy of etanercept (0.8 mg/kg) for treating moderate to severe plaque psoriasis in pediatric patients enrolled at 4 to 17 years of age.

METHODS

Study design

This study (study 20050111) was an OLE of the parent 20030211 study (ClinicalTrials.gov no. NCT00078819), a 48-week study that enrolled 211 patients with moderate to severe plaque psoriasis between 4 and 17 years of age.[14] The parent study was conducted in 3 consecutive phases: a 12-week double-blind, placebo-controlled phase; a 24-week open-label phase; and a 12-week double-blind withdrawal-retreatment phase (Supplemental Fig 1; available at http://www.jaad.org).[14] During the OLE study, patients received etanercept once weekly at 0.8 mg/kg (maximum 50 mg) for up to 264 weeks. Use of topical standard-of-care therapy, including mild- to moderate-potency topical corticosteroids, was allowed during the study. Patients were allowed to discontinue etanercept from week 96 if they had a static physician global assessment (sPGA) status of clear/almost clear (score of 0/1), and could restart etanercept at the discretion of the investigator. An interim analysis at week 96 has been reported.[15] Patients who enrolled in the OLE study were followed up through week 264 or until they turned 18 years of age, whichever came last.

The study was conducted in accordance with International Conference on Harmonization Good Clinical Practice regulations and guidelines and with the Declaration of Helsinki. Institutional review boards at each participating site approved the study protocol and amendments, and written informed consent was provided by parents or legal guardians of each patient before initiation of study-related procedures. This study was registered under ClinicalTrials.gov no. NCT00141921 on August 31, 2005, and the first patient was enrolled on August 11, 2005. This analysis includes data through February 22, 2012.