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# Etanercept in children with polyarticular juvenile rheumatoid arthritis

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## Keywords

Etanercept, polyarticular juvenile chronic arthritis, soluble tumor necrosis factor receptor fusion protein, tumor necrosis factor blocker

# Context

Juvenile rheumatoid arthritis (JRA) is a group of diseases, classified as systemic onset, pauciarticular or polyarticular JRA. The latter form can be further divided on the basis of the presence of rheumatoid factor. Polyarticular JRA differs from the adult type with respect to several characteristics such as prevalence, prognosis and response to therapy. In one third of the patients, the disease is controlled with nonsteroidal antiinflammatory drugs and physical and occupational therapy. The remainder are candidates for more aggressive therapy such as sulfasalazine and methotrexate, but some patients do not respond adequately even at doses up to 1 mg methotrexate per kilogram of body weight per week. As in the adult form of arthritis, tumor necrosis factor (TNF) is elevated in serum and synovial fluid of patients with JRA. Serum levels of the soluble TNF-receptor are elevated in these patients and the level correlates with disease activity. The introduction of TNF inhibitors in the treatment of adult patients with RA who did not respond to standard disease-modifying drugs has resulted in a significant clinical benefit with minimal toxicity. This multicenter study evaluated the efficacy and safety of etanercept, a soluble TNF-receptor, in children with polyarticular JRA.

# Significant findings

All 69 patients initially received treatment with etanercept 0.4 mg/kg subcutaneously twice weekly in an open label fashion. After 3 months 51 patients (74%) had a response, defined as 30% improvement from baseline in at least three of six variables. These 51 patients entered the randomized and double-blind study of etanercept versus placebo. The primary efficacy endpoint was the proportion of patients who withdrew from the study because of a disease flare. Disease flare was defined as worsening of 30% or more in three of the six response variables with a minimum of two active joints. This definition did not require the disease to become as active as baseline. In 21 of the 26 patients (81%) on placebo a flare occurred, as compared with 7 of 25 (28%) who received etanercept ($p = 0.003$). The median time to disease flare with placebo was 28 days as compared with more than 116 days with etanercept ($p <$ 0001). In the double-blind study there were no significant differences in the frequencies of adverse events between patients who received etanercept and those who received placebo.

# Comments

This clinical trial used an unusual protocol, as all patients received treatment with the active compound etanercept in the first phase of the study. Patients who responded to treatment entered the double blind part of the study and were randomly assigned to receive placebo or etanercept. With this design patients are soon aware of whether treatment with the active compound has an effect. This design could also be applied to studies in adults.

# Methods

A group of 69 children with JRA who had active disease and did not tolerate or did not have an adequate response to methotrexate were treated with etanercept. Those who responded entered the double-blind study and were randomly assigned to receive placebo or etanercept for 4 months or until a flare occurred.

# Additional information

## References

1. Lovell DJ, Giannini EH, Reiff A, Cawkwell GD, Silverman ED, Nocton JJ, Stein LD, Gedalia A, Ilowite NT, Wallace CA, Whitmore J, Finck BK: Treatment with etanercept leads to a significant improvement in children with polyarticular juvenile rheumatoid arthritis and is safe and well tolerated. N Engl J Med. 2000, 342: 763-769.