Tocilizumab Improves Systemic Juvenile Arthritis

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VIENNA — Blockade of the interleukin-6 receptor using the investigational biologic agent tocilizumab shows considerable early promise as a novel treatment for systemic juvenile idiopathic arthritis, Patricia Woo, M.D., said at the annual European congress of rheumatology.

Tocilizumab is the first anti-interleukin (IL)-6 receptor antibody. This humanized monoclonal antibody is now in phase III clinical trials for treatment of rheumatoid arthritis and several other rheumatologic diseases in adults. Dr. Woo and her coinvestigators reasoned that IL-6 signaling is also a rational therapeutic target in systemic juvenile idiopathic arthritis (sJIA), since serum IL-6 levels are known to be greatly elevated in youths with that disorder.

Dr. Woo reported on 18 patients with sJIA who participated in a phase II Chugai Pharma-sponsored clinical trial in which they received a single dose of tocilizumab. All the children required more than 0.2 mg/kg per day of systemic corticosteroids at baseline. Participants were allowed to be on methotrexate at up to 20 mg/m² per week, but all other disease-modifying drugs were phased out prior to their participation in the investigation.

A single-dose trial was all that the British ethics committee was willing to authorize in children at that point in the drug’s development, despite the fact that sJIA is a serious disease often unresponsive to anything other than chronic systemic corticosteroids, with their attendant serious side effects, explained Dr. Woo, professor of pediatric rheumatology at Great Ormond Street Hospital, London.

An estimated 10%-15% of juvenile idiopathic arthritis patients have the sJIA form, characterized by high fevers, rash, and intensely painful swollen joints. “This is a disease that has a degree of mortality,” she noted at the meeting, which was sponsored by the European League Against Rheumatism.

Half of the study participants were aged 2-5 years; the other half were aged 6-18 years. None had their disease under satisfactory control with available therapies. One-third of them received 2 mg/kg of tocilizumab by intravenous infusion, another third received 4 mg/kg, and the rest received 8 mg/kg.

All 18 patients experienced clinical improvement within 48 hours. Thirteen showed at least a 30% improvement in the core features of sJIA within 1 week.

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The magnitude and duration of response were greater with higher doses of tocilizumab. For example, four of six patients who received the 4 mg/kg dose experienced at least a 50% improvement in symptoms within a week, including two who had a 70% improvement.

The clinical improvement was paralleled by a drop in C-reactive protein levels.

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Drug-related adverse events occurred in four patients. They included an infusion reaction, a case of transient pancytopenia, a disease flare accompanied by herpes simplex, a case of varicella in a child exposed to a day-care outbreak, and transient elevations in liver enzymes in three patients also on methotrexate, all of whom had previously experienced hepatic enzyme elevations while on methotrexate alone. There were no serious bacterial infections.

Dr. Woo said that based on these very encouraging early findings, she intends to enroll patients in an international phase III placebo-controlled trial of tocilizumab for sJIA now being planned. A similar study is already underway in Japan.