Anakinra Suited to Children With Systemic JIA

BY AMY ROTHMAN SCHONFELD

NEW YORK — New evidence that children with the systemic form of juvenile idiopathic arthritis respond better to treatment with anakinra than do those with other types of arthritis lends credence to the hypothesis that a different pathway underlies systemic disease, according to Dr. Norman T. Ilowite.

In an open-label study, the response rate was 73% (11 of 15) for children with systemic juvenile idiopathic arthritis (JIA), compared with 67% (6 of 9) for children with pauciarticular and 52% (29 of 56) for children with polyarticular JIA.

The overall response rate was 58% (46 of 80), according to Dr. Ilowite, who reported his findings at a rheumatology meeting sponsored by New York University.

"These observations are in contradistinction to those seen in most studies of [tumor necrosis factor] therapies in JIA, where those with systemic disease didn't do as well as those with polyarticular or oligoarticular disease," said Dr. Ilowite, chief of pediatric rheumatology at Children's Hospital at Montefiore Medical Center and professor of pediatrics at the Albert Einstein College of Medicine, both in New York.

Anakinra is similar to a naturally occurring interleukin-1 (IL-1) receptor antagonist that has been approved for the management of signs and symptoms of rheumatoid arthritis in adults. It has not received approval for use in children with arthritis.

It has been proposed that inflammation in systemic JIA is mediated by IL-1, and thus that the inhibition of IL-1's proinflammatory effects would be an attractive therapeutic strategy.

Systemic JIA appears to be similar to other autoinflammatory syndromes in which IL-1 inhibition has been used successfully as therapy, including neonatal-onset multisystem inflammatory disease (NOMID) and cryopyrin-associated periodic syndromes (CAPS), said Dr. Ilowite.

Although the number of patients enrolled was small, Dr. Ilowite also presented data suggesting that anakinra was safe and reduced the number of disease flares across all subtypes of JIA, compared with placebo (Clin. Rheumatol. 2009;28:129-37).

TNF blockers have tended to work better in children whose JIA is polyarticular or oligoarticular in nature. Anakinra seems to work better in systemic JIA.

Systemic JIA affects about 10% of children who have JIA, said Dr. Ilowite. It is the only subtype that causes fever, and arthritis usually ensues within 6 months of fever onset. It begins with mostly extra-articular manifestations, and is the only subtype with no strong HLA, sex, or age predilections.

The course is highly variable, with about 40% following a uniphasic course that fades within about 2 years, about 55% following a persistent course that progresses rapidly with serious systemic manifestations, and about 5% having intermittent exacerbations and remissions. Extra-articular manifestations include daily fever with two spikes a day, hepatosplenomegaly, lymphadenopathy, and rash.

Macrophage activation syndrome, a potentially fatal complication, occurs in about 7% of children with systemic JIA, according to Dr. Ilowite.

Other studies also suggest a preferential importance of IL-1 pathway activation in systemic JIA.

Anakinra was effective in a retrospective study of 33 patients with systemic JIA (J. Clin. Rheumatol. 2009;15:161-4). Furthermore, a characteristic IL-1 signature was reversed among systemic JIA patients who were treated with anakinra (J. Exp. Med. 2005;201:1479-86). ■

Disclosures: *Dr. Ilowite had nothing to disclose. His study is reporting on unapproved indications for anakinra.*