# Anakinra Shows Benefit for Systemic-Onset JIA

BY JANE SALODOF MACNEIL
*Southwest Bureau*

VERSAILLES, FRANCE — Anakinra (Kineret) is effective against systemic-onset juvenile idiopathic arthritis, Marilynn Punaro, M.D., reported at the annual scientific meeting of the European Pediatric Rheumatology Congress.

Twelve of 13 children treated at Texas Scottish Rite Hospital for Children in Dallas responded to anakinra, an interleukin-1 receptor antagonist, according to a retrospective chart review presented by Dr. Punaro of the University of Texas Southwestern Medical School at Dallas.

Fever resolved immediately in most cases. Arthritis symptoms improved more slowly, but Dr. Punaro reported they had largely abated at an average follow-up of 14 months.

Eight children had complete sustained responses, she said. Two children, described as "substantially improved," had partial sustained responses. Dr. Punaro noted that one went from active involvement of 34 joints to just two active joints.

Two others, who had complete transient responses, flared after infections. Only one child, described as "the most persistently active patient," did not benefit and has been taken off drug for lack of efficacy.

**Side effects did not increase with higher doses in initial nonresponders. 'The real question here is, what is the dose? Nobody knows the answer to that.'**

The children, nine girls and four boys, ranged in age from 2 to 17 years when they started on anakinra. Their average duration of disease was 44 months, with a range of 1-142 months. Four were having flares at the initiation of anakinra, according to Dr. Punaro.

Before anakinra therapy, most patients were taking other agents, including corticosteroid, intravenous methylprednisone and/or methotrexate. Two children discontinued infliximab when they started on anakinra.

After anakinra, none of the children continued intravenous methylprednisone, according to Dr. Punaro. Physicians were able to taper the doses of all 11 children on corticosteroids.

While injection site complaints were common, she said infections were a major problem. These include three cases of upper respiratory tract infections, two of influenza, and one each of gastroenteritis, staphylococcus skin infection, and possible sepsis. Dr. Punaro noted that most patients continued on anakinra during infections against medical advice.

She said side effects did not increase with dose increases in children who did not respond initially. "The real question here is, what is the dose?" she said. "Nobody knows the answer to that."

Microarray analyses showed a direct correlation between degree of clinical and genetic responses, Dr. Punaro added. She showed microarrays for three complete responders in which a genetic signature for systemic-onset juvenile idiopathic arthritis was virtually suppressed. Changes in gene expression were less dramatic by comparison in children with lesser responses.

"These are very preliminary data, but they suggest that [anakinra] may be useful," she said. ■



# Twelve Genes Distinguish SOJIA From Other Inflammatory Ills

VERSAILLES, FRANCE — Investigators at the Baylor Institute for Immunology Research in Dallas have identified 12 genes that can distinguish systemic-onset juvenile idiopathic arthritis from other inflammatory conditions as well as from healthy controls.

The genes are part of a newly discovered 88-gene signature for systemic-onset juvenile idiopathic arthritis (SOJIA), Virginia Pascual, M.D., reported in a presentation at the 12th European Pediatric Rheumatology Congress.

"Most of them are genes that have not been characterized. I wish I could tell you more. It is not that I want to hide them," she told audience members who sought more information.

Dr. Pascual, who is also affiliated with the Texas Scottish Rite Hospital for Children in Dallas, said the researchers initially identified 50 genes associated with the disease by comparing 873 genes in microarrays from 44 SOJIA patients.

Among the SOJIA patients, 16 (group 1) presented with fever and arthritis. Nine (group 2) had recovered from fever but still had arthritis. Nineteen intermittent patients were in remission (group 3) and did not have fever or arthritis.

Distinguishing microarrays of the SOJIA patients from those of healthy controls turned out to be easy, according to Dr. Pascual. She reported that the investigators were able to identify group 1 with 100% accuracy, group 2 with 96% accuracy, and the patients in remission with 86% accuracy.

The "diagnostic challenge" was not to distinguish SOJIA patients from healthy children, she continued, but from those with other inflammatory conditions. When investigators looked at arrays from children with *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli,* influenza A, and systemic lupus erythematosus, it became apparent that many of the same genes were overexpressed in these other conditions as well as in SOJIA.

"Many genes that we find are shared by all these conditions, so we have to dig deeper, and we have done it," she said.

To find genes more specific to SOJIA, the researchers screened 4,311 genes, which they eventually refined to the 88-gene signature. Among these, Dr. Pascual reported 12 appeared to be enough to distinguish SOJIA patients not only from healthy controls but also from those with the other infectious diseases; lupus; and pyogenic arthritis, pyoderma gangrenosum, and acne (PAPA) syndrome. The genes in the signature "seem to be specific so far. They are very stable," she said.

Among patients with active disease, those with a full clinical response to treatment also had a significant change in the signature, according to Dr. Pascual. Meanwhile, patients with weaker clinical responses showed lesser changes in the genetic signature.

"We are very interested in following these patients," Dr. Pascual said of the ongoing investigation. "It is going to be very important to find markers that can predict response to therapy."

**—Jane Salodof MacNeil**