

# Anakinra Shows Benefit for Systemic-Onset JIA

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VERSAILLES, FRANCE — Anakinra (Kineret) is effective against systemic-onset juvenile idiopathic arthritis, Marilyn 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.

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. ■

<b>Respiratory</b>	asthma, bronchospasm, dyspnea
<b>Skin and Appendages</b>	alopecia, angioedema, bullous eruption, erythema multiforme, photosensitivity reaction, pruritus, exfoliative dermatitis, Stevens-Johnson syndrome, sweating increased, toxic epidermal necrolysis, urticaria
<b>Special Senses</b>	abnormal vision, conjunctivitis, taste perversion, tinnitus
<b>Urinary System</b>	albuminuria, BUN increased, creatinine increased, hematuria, interstitial nephritis, renal failure

#### OVERDOSAGE

There is limited experience with meloxicam overdose. Four cases have taken 6 to 11 times the highest recommended dose; all recovered. Cholestyramine is known to accelerate the clearance of meloxicam.

Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Severe poisoning may result in hypertension, acute renal failure, hepatic dysfunction, respiratory depression, coma, convulsions, cardiovascular collapse, and cardiac arrest. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed with symptomatic and supportive care following an NSAID overdose. In cases of acute overdose, gastric lavage followed by activated charcoal is recommended. Gastric lavage performed more than one hour after overdose has little benefit in the treatment of overdose. Administration of activated charcoal is recommended for patients who present 1-2 hours after overdose. For substantial overdose or severely symptomatic patients, activated charcoal may be administered repeatedly. Accelerated removal of meloxicam by 4 gm oral doses of cholestyramine given three times a day was demonstrated in a clinical trial. Administration of cholestyramine may be useful following an overdose. Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

#### DOSAGE AND ADMINISTRATION

##### Osteoarthritis and Rheumatoid Arthritis

Carefully consider the potential benefits and risks of MOBIC and other treatment options before deciding to use MOBIC. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see **WARNINGS**).

After observing the response to initial therapy with MOBIC, the dose should be adjusted to suit an individual patient's needs.

For the relief of the signs and symptoms of osteoarthritis the recommended starting and maintenance oral dose of MOBIC is 7.5 mg once daily. Some patients may receive additional benefit by increasing the dose to 15 mg once daily. For the relief of the signs and symptoms of rheumatoid arthritis, the recommended starting and maintenance oral dose of MOBIC is 7.5 mg once daily. Some patients may receive additional benefit by increasing the dose to 15 mg once daily.

MOBIC oral suspension 7.5 mg/5 mL or 15 mg/10 mL may be substituted for MOBIC tablets 7.5 mg or 15 mg, respectively.

The maximum recommended daily oral dose of MOBIC is 15 mg regardless of formulation.

##### Pauciarticular and Polyarticular Course Juvenile Rheumatoid Arthritis (JRA)

MOBIC oral suspension is available in the strength of 7.5 mg/5 mL. To improve dosing accuracy in smaller weight children, the use of the MOBIC oral suspension is recommended. For the treatment of juvenile rheumatoid arthritis, the recommended oral dose of MOBIC is 0.125 mg/kg once daily up to a maximum of 7.5 mg. There was no additional benefit demonstrated by increasing the dose above 0.125 mg/kg once daily in these clinical trials.

**Juvenile Rheumatoid Arthritis dosing using the oral suspension should be individualized based on the weight of the child:**

Weight	0.125 mg/kg	
	Dose (1.5 mg/mL)	Delivered dose
12 kg (26 lb)	1.0 mL	1.5 mg
24 kg (54 lb)	2.0 mL	3.0 mg
36 kg (80 lb)	3.0 mL	4.5 mg
48 kg (106 lb)	4.0 mL	6.0 mg
≥60 kg (132 lb)	5.0 mL	7.5 mg

**Shake the oral suspension gently before using.**

MOBIC may be taken without regard to timing of meals.

**Rx only**

MB-BS (08/05) 10003990/US/1



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Printed in U.S.A. (08/05)

MB-10982

## 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