

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 contradiction 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, com-

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.

pared with placebo (Clin. Rheumatol. 2009;28:129-37).

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.

Colcrys
(colchicine, USP) tablets

COLCRYS® (colchicine, USP) tablets for oral use

Brief Summary of full Prescribing Information

The following is a brief summary only. Please see full Prescribing Information for complete product information.

INDICATIONS AND USAGE

COLCRYS® (colchicine, USP) tablets are indicated for prophylaxis and the treatment of gout flares.

Prophylaxis of Gout Flares: COLCRYS is indicated for prophylaxis of gout flares.

Treatment of Gout Flares: COLCRYS is indicated for treatment of acute gout flares when taken at the first sign of a flare.

Familial Mediterranean fever (FMF): COLCRYS is indicated in adults and children 4 years or older for treatment of familial Mediterranean fever (FMF).

CONTRAINDICATIONS

Patients with renal or hepatic impairment should not be given COLCRYS in conjunction with P-gp or strong CYP3A4 inhibitors. In these patients, life-threatening and fatal colchicine toxicity has been reported with colchicine taken in therapeutic doses.

WARNINGS AND PRECAUTIONS

Fatal Overdose: Fatal overdoses, both accidental and intentional, have been reported in adults and children who have ingested colchicine. COLCRYS should be kept out of the reach of children.

Blood Dyscrasias: Myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, and aplastic anemia have been reported with colchicine used in therapeutic doses.

Drug Interactions: Colchicine is a P-gp and CYP3A4 substrate. Life-threatening and fatal drug interactions have been reported in patients treated with colchicine given with P-gp and strong CYP3A4 inhibitors. If treatment with a P-gp or strong CYP3A4 inhibitor is required in patients with normal renal and hepatic function, the patient’s dose of colchicine may need to be reduced or interrupted [see *DRUG INTERACTIONS*]. Use of COLCRYS in conjunction with P-gp or strong CYP3A4 inhibitors is contraindicated in patients with renal or hepatic impairment [see *CONTRAINDICATIONS*].

Monitor for toxicity and if present consider temporary interruption or discontinuation of COLCRYS.

Neuromuscular Toxicity: Colchicine-induced neuromuscular toxicity and rhabdomyolysis have been reported with chronic treatment in therapeutic doses. Patients with renal dysfunction and elderly patients, even those with normal renal and hepatic function, are at increased risk. Concomitant use of atorvastatin, simvastatin, pravastatin, fluvastatin, gemfibrozil, fenofibrate, fenofibric acid, or bezafibrate (themselves associated with myotoxicity) or cyclosporine with COLCRYS may potentiate the development of myopathy [see *DRUG INTERACTIONS*]. Once colchicine is stopped, the symptoms generally resolve within 1 week to several months.

ADVERSE REACTIONS

Prophylaxis of Gout Flares: The most commonly reported adverse reaction in clinical trials of colchicine for the prophylaxis of gout was diarrhea.

Treatment of Gout Flares: The most common adverse reactions reported in the clinical trial with COLCRYS for treatment of gout flares were diarrhea (23%) and pharyngolaryngeal pain (3%).

FMF: Gastrointestinal tract adverse effects are the most frequent side effects in patients initiating COLCRYS, usually presenting within 24 hours, and occurring in up to 20% of patients given therapeutic doses. Typical symptoms include cramping, nausea, diarrhea, abdominal pain, and vomiting. These events should be viewed as dose-limiting if severe as they can herald the onset of more significant toxicity.

DRUG INTERACTIONS

COLCRYS is a substrate of the efflux transporter P-glycoprotein (P-gp). Of the cytochrome P450 enzymes tested, CYP3A4 was mainly involved in the metabolism of colchicine. If COLCRYS is administered with drugs that inhibit P-gp, most of which also inhibit CYP3A4, increased concentrations of colchicine are likely. Fatal drug interactions have been reported. Physicians should ensure that patients are suitable candidates for treatment with COLCRYS and remain alert for signs and symptoms of toxicities related to increased colchicine exposure as a result of a drug interaction. Signs and symptoms of COLCRYS toxicity should be evaluated promptly and, if toxicity is suspected, COLCRYS should be discontinued immediately. See full Prescribing Information for a complete list of reported potential interactions.

USE IN SPECIFIC POPULATIONS

- In the presence of mild to moderate renal or hepatic impairment, adjustment of dosing is not required for treatment of gout flare, prophylaxis of gout flare, and FMF but patients should be monitored closely.
- In patients with severe renal impairment for prophylaxis of gout flares the starting dose should be 0.3 mg/day, for gout flares no dose adjustment is required but a treatment course should be repeated no more than once every 2 weeks. In FMF patients, start with 0.3 mg/day and any increase in dose should be done with close monitoring.
- In patients with severe hepatic impairment, a dose reduction may be needed in prophylaxis of gout flares and FMF patients; while a dose reduction may not be needed in gout flares, a treatment course should be repeated no more than once every 2 weeks.
- For patients undergoing dialysis, the total recommended dose for prophylaxis of gout flares should be 0.3 mg given twice a week with close monitoring. For treatment of gout flares, the total recommended dose should be reduced to 0.6 mg (1 tablet) x 1 dose and the treatment course should not be repeated more than once every two weeks. For FMF patients the starting dose should be 0.3 mg per day and dosing can be increased with close monitoring.
- Pregnancy: Use only if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: Caution should be exercised when administered to a nursing woman.
- Geriatric Use: The recommended dose of colchicine should be based on renal function.

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