Longer treatment for juvenile arthritis during remission does not reduce relapse rate

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For patients with juvenile idiopathic arthritis in remission, withdrawal of treatment with the drug methotrexate over 12 months vs. 6 months did not reduce the rate of relapse, according to a study in the April 7 issue of *JAMA*.

New therapies have improved the remission rate in chronic inflammatory disorders such as juvenile idiopathic arthritis (JIA; persistent or recurring inflammation of the joints similar to rheumatoid arthritis but beginning at or before age 16). "… physicians have to balance the risk of doing too little (e.g., withdrawing medication and provoking flares [relapses]) vs. the risk of doing too much (e.g., continuing medication despite a stable remission and thereby accepting the risk of adverse effects). While evidence-based advice for starting therapies in active disease is available, no controlled data exist to suggest the need for treatment continuation after remission is achieved," the authors write.

Dirk Foell, M.D., of the University of Muenster, Germany, and colleagues analyzed whether the duration of methotrexate therapy during clinical remission of JIA influences the rate of flares after withdrawal, and also examined whether patients at risk for a flare may be identified with use of the biomarker myeloid-related protein (MRP) 8 and MRP 14 (MRP8/14), which has been shown to be a marker of subclinical disease activity not detectable by laboratory tests. The randomized clinical trial included 364 patients (median [midpoint] age, 11.0 years) with JIA recruited in 61 centers from 29 countries between February 2005 and

June 2006. Patients were included at first confirmation of clinical remission while continuing medication. At the time of therapy withdrawal, levels of MRP8/14 were determined.

Patients were randomly assigned to continue with methotrexate therapy for either 6 months (group 1 [n = 183]) or 12 months (group 2 [n = 181]) after the beginning of disease remission.

Analyses indicated relapse within 24 months after the inclusion into the study in 98 of 183 patients (56.7 percent) in group 1 and 94 of 181(55.6 percent) in group 2. The median relapse-free interval after inclusion was 21 months in group 1 and 23 months in group 2. Median follow-up duration after inclusion was 34.2 and 34.3 months in groups 1 and 2, respectively. In the 297 patients who stopped therapy while in remission, 39.6 percent in group 1 and 39.5 percent in group 2 had a flare within 1 year.

"Levels of MRP8/14 during remission were significantly higher in patients who subsequently developed flares compared with patients maintaining stable remission. Low MRP8/14 levels indicated a low risk of flares within the next 3 months following the biomarker test," the authors write.

"These data indicate a need for the stratification of patients with chronic inflammatory diseases to ensure that the intensity of treatment is adjusted to the patients' individual needs."

The researchers add that it cannot be recommended that methotrexate therapy be continued in all patients for longer than 6 months after remission is induced.

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