Philadelphia
Extending methotrexate for more than 6 months after
induction of remission had no added benefit for preventing long-term flares in a randomized study of more than 300 pa-
tients with rheumatoid arthritis.

The findings also showed that treating serum levels of the inflammatory
marker myeloid-related protein (MRP)8/14 predicted which patients in remission would experience flares off treatment and which would not.

Based on these results, MRP8/14 now is routinely used at the University of Muenster (Germany) to guide withdrawal of methotrexate from JA pa-
tients. Dr. Doefl said at the annual meeting of the American College of Rheumatology.

“This is the first controlled trial ana-

alyzing the necessary time of treatment continuation once remission is achieved in a rheumatic disease,” said Dr. Doefl, a pediatric rheumatologist at the universi-

ity. Continuing methotrexate longer than 6 months after achieving clinical remis-

sion “does not influence the risk of JA relapse and can improve treatment outcomes in general,” he said. However, some pa-
tients may reach an unstable remission on medication, giving them a status of clinical but not immunologic remission. “MRP8/14, a marker of phagocyte activity, indicates subclinical inflammation and identifies patients with an increased risk of relapse in whom therapy may not be safely stopped,” said Dr. Doefl.

The researchers proposed a MRP8/14 cut-off of 690 ng/dl—"the level now used in Muenster to guide methotrexate with-

drawal—because it combined the best level of specificity and sensitivity for pre-

dicting relapse. But they recognize that the statistical cutoff is not ideal for all cases.

Dr. Doefl and his colleagues continue to look for more intelligent markers of inflammation to detect at-risk patients, he added.

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A multicenter collaboration of PRINeto (Pediadiatric Rheumatology Inter-

ational Trials Organization) randomized 364 JA patients with clinical re-
misston on methotrexate. The average age of the patients was 11 years, about two-thirds were girls, nearly 90% were white, and their median disease duration at enrollment was 3 years. The re-

searchers took patients off methotrexate after either 6 or 12 months of remission. They took serum specimens from 188 patients (52%) just before cessation of methotrexate therapy to measure MRP8/14, which is very reliable in the same serum.

In a intent-to-treat analysis, the rates of relapse in patients with a MRP8/14 levels of 690 ng/dl or more were 17% and 22% for the first and second 6-month periods of follow-up, respectively. Relapse rates of patients with a MRP8/14 levels of 690 ng/dl or more were 17% and 22% for the first and second 6-month periods of follow-up, respectively.

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The relapse rates of patients with low or high MRP8/14 levels began to diver-

diate in the first months of methotrexate withdraw-

al, and continued to steadily diverge after that.

This investigator-initiated study received no major industry support, said Dr. Foell; it did receive some funding from Wyeth Pharmaceuticals, the German Rheumatology League, and PRINeto. Dr. Foell disclosed that he was a scientific adviser to Wyeth, Re-
generon Pharmaceuticals Inc., and Cis-

Bio International.