



# ACR Hotline

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## Methotrexate for Giant Cell Arteritis

Treatment with corticosteroids (CS) is usually dramatically effective in the management of active giant cell arteritis (GCA). Doses of prednisone equivalent of 40-60 mg a day are usually used at the outset of treatment, with tapering of the dose according to symptoms over an average of 2-3 years. A majority of patients have at least one relapse during treatment, and side effects of long-term CS use in the doses required for control of the disease are seen in 60-80% of patients, with attendant implications for quality of life and need for medical services. In spite of this, most studies of survivorship in GCA have not shown a diminished life expectancy in these patients compared to the general population.

In an effort to reduce the CS related side effects, numerous adjuvant therapies have been employed by physicians treating this disease in an anecdotal fashion, particularly azathioprine and methotrexate, without clear-cut evidence of their efficacy. This issue is of great interest to practicing rheumatologist, and the subject of two recent studies. At the 2000 ACR Annual Scientific Meeting in Philadelphia, results of two trials of methotrexate (MTX) for this indication were reported. One of these, authored by Jover and colleagues from Madrid, Spain, has since been published (*Ann Intern Med* 2001;134:106-11). The other, a multicenter multinational trial authored by Hoffman and colleagues, is in press.

Both studies were randomized and placebo controlled. 98 patients with new onset GCA were enrolled in the Hoffman trial (51 MTX + CS; 47 placebo + CS), and 42 (21 MTX + CS; 21 placebo + CS) patients with new onset GCA who had not received more than 10 mg prednisone/day for the 2 weeks preceding enrollment were entered in the Jover trial. The initial dose of prednisone was 60 mg/day in the Jover trial, and 1mg/kg/d, up to 60 mg/day in the Hoffman trial. Initial MTX dose in the Jover trial was 10 mg/wk; this dose was maintained throughout the 24 month trial. The initial dose of MTX in the Hoffman trial was 0.15 mg/kg/wk and increased to as much as 0.25 mg/kg/wk but not exceeding 15 mg/week total dose for the 12 month duration of the trial.

In the Jover study, 12 relapses occurred in 9 patients (43% by intent-to-treat analysis, but only 15 patients actually completed the trial) in the MTX group, and 26 relapses occurred in 16 patients (76% by intent-to-treat; 18 patients completed the trial) in the placebo group. Most relapses occurred within the first 30 weeks of treatment. The mean cumulative dose of prednisone was  $4187 \pm 1529$  mg in the MTX group and  $5489.5 \pm 1396$  in the placebo group (a difference of 1302 mg,  $p = 0.009$ ). The authors reported that 3 patients were withdrawn for MTX related side effects, and a total of 5 patients in the MTX group were withdrawn prematurely; 1 patient in the placebo group was withdrawn prematurely. The rate of CS related side effects was similar in both groups.

In contrast, the Hoffman study found no difference between the number of relapses and treatment failures (MTX 54%, placebo 68%;  $p=0.42$ ), and there were no differences in cumulative CS doses between groups. Like the Jover study, there was no difference between groups in CS related toxicity, and the Hoffman study found no differences between overall treatment toxicities between groups.

Both studies had similar numbers of relapses in the MTX treated and placebo treated groups, although the magnitude of difference was greater in the Jover study in this cohort of a much smaller number of patients. The data about whether MTX has a steroid sparing effect or efficacy in GCA are limited and underscore the need for more well done clinical trials with an appropriate sample size to better resolve this issue.

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Hotline Editors