Methotrexate/Tocilizumab Combo Offers New Option for RA

BY DIANA MAHONEY

COPENHAGEN—The addition of tocilizumab to methotrexate therapy is a promising new option for rheumatoid arthritis patients who do not fully respond to treatment with the disease-modifying antirheumatic drug alone, Dr. Joel M. Kremer said at the annual European Congress on Rheumatology.

Dr. Kremer, director of research at the Center for Rheumatology LLC in Albany, N.Y., presented 1-year data from the international LITHE (Tocilizumab Safety and the Prevention of Structural Joint Damage) study showing that the anti–interleukin-6 monoclonal antibody inhibits structural joint damage and improves physical function and clinical disease activity, compared with methotrexate alone.

The randomized, double-blind, placebo-controlled LITHE study, which was sponsored by Roche, enrolled 1,196 patients with moderate to severe rheumatoid arthritis who had an inadequate response to methotrexate. Patients were randomized to receive a 4-mg/kg or 8-mg/kg infusion of tocilizumab (Actemra) every 4 weeks in combination with stable doses of methotrexate or methotrexate/placebo. The study’s primary end points included ACR 20 response at 24 weeks and change from baseline in Genant-modified Total Sharp Score (GmTSS) and physical function at 52 weeks, measured by area under the curve (AUC) of change from baseline in the Health Assessment Questionnaire Disability Index (HAQ-DI), Dr. Kremer explained.

At 24 weeks, ACR 20 response was achieved by 56% and 51%, respectively, in the tocilizumab 8-mg and 4-mg combination therapy groups, compared with 27% of the methotrexate-only group. Dr. Kremer said, noting that significantly more patients in combination therapy groups achieved ACR 20/50/70 responses at week 52.

Also at 52 weeks, there were significantly more patients in the combination therapy groups without radiographic progression from baseline, compared with the methotrexate-only group. Total GmTSS change from baseline was –24 points in the methotrexate/tocilizumab group, –27 points in the tocilizumab (4 mg)/methotrexate group, and –30 points in the methotrexate-only group. The respective percentages of patients achieving no progression in GmTSS were 85%, 81%, and 67%, respectively.

In particular, patients must be monitored for abnormalities in transaminase enzymes, which could require an adjustment in the dose of either medication, Dr. Kremer said. In the event of significant increases in lipid levels in a patient with underlying risk factors for cardiovascular disease, strong consideration should be given to the initiation of a statin agent, he said.

“Tocilizumab represents a new approach to treating severe arthritis, but as always, the decision to use a particular biologic agent is not cast in stone” Dr. Kremer said in an interview. “There will always be patients in any busy practice who have tried and failed the multiple agents previously available. In these patients, he said, “trying a new mechanism of action, while watching carefully for the emergence of side effects, is reasonable.”

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Dr. Kremer, who is also the founder and president of CORRONA (Consortium of Rheumatology Researchers of North America), disclosed that he has received grants for clinical research from—and has served as a consultant for—Abbott Laboratories, Amgen Inc., Bristol-Myers Squibb Co., Centocor Inc., Genentech Inc., and Roche.