Combo Helps Early RA Patients Attain Remission

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BOSTON — Half of patients with early rheumatoid arthritis treated with a combination of etanercept and methotrexate achieved disease remission within 1 year in the first major trial to use remission as the primary end point, Dr. Paul Emery reported in a late-breaking abstract session at the annual meeting of the American College of Rheumatology.

"We have been talking about remission for a long time," said Dr. Emery, who wrote a viewpoint piece more than a decade ago entitled "Early rheumatoid arthritis: Time to aim for remission?" (Ann. Rheum. Dis. 1995;54:944-7). "We now can say this is a realistic goal."

The trial, known as COMET (Combination of Methotrexate and Etanercept in Active Early Rheumatoid Arthritis), compared the clinical efficacy and safety of etanercept plus methotrexate with methotrexate alone in a randomized, double-blind study that included 542 adult patients from 22 countries.

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Trial participants had active disease as determined by a Disease Activity Score–28 (DAS28) of 3.2 or greater, and elevations either of erythrocyte sedimentation rate (ESR) to 28 mm/hr or higher or of C-reactive protein to 20 mg/L or more. All of the patients were methotrexate naive and had a disease duration of 2 years or less.

Baseline demographics and disease characteristics were similar in the etanercept plus methotrexate and methotrexate-alone groups. Mean age was 51 years, and median disease duration was 7 months in both groups. Mean baseline DAS28 was 6.5, so the DAS28 was high despite the short disease duration, said Dr. Emery.

About half had received corticosteroids, and 22% had previously been treated with a disease-modifying antirheumatic drug other than methotrexate.

The primary end point of remission (defined as a DAS28 less than 2.6) was achieved by 50% of patients on combination therapy by week 52, compared with 28% of patients receiving methotrexate alone. This represented a statistically significant difference, and "a considerable achievement," said Dr. Emery, professor of rheumatology at the University of Leeds (England).

Low disease activity (defined as a DAS28 of 3.2 or less) was achieved by week 52 by 64% and 41% of patients in the combination and methotrexate groups, respectively, which also was a statistically significant difference. Moreover, it was "quite remarkable" how quickly remission was achieved, with significant differences being seen at 2 weeks, he said.

By weeks 16-20, 40% of patients in the combination group were in remission, he said. "This is a new standard of speed for achieving remission," he noted.

Responses on the American College of Rheumatology (ACR) scales were evaluated as secondary end points. "It's traditional with most biologics to expect ACR 20, 50, and 70 responses of 60%, 40%, and 20%, but with the combination we saw response rates of 86%, 71%, and 48%, which are very high rates indeed," Dr. Emery commented.

These levels of ACR response were seen in 67%, 49%, and 28% of the methotrexate group. Levels of C-reactive protein improved dramatically by week 2 and stabilized by week 16. By week 52, 55% of patients had normal Health Assessment Questionnaire (HAQ) scores, meaning that they had normal functional status. There also was a two-thirds reduction in workdays lost, which is important from a cost point of view, he said.

"Finally, there were no new safety signals associated with combination therapy, which is terribly important for patients who are naive to methotrexate," he said.

Serious adverse events were reported by 12% of patients in the combination group and by 13% of patients in the methotrexate group. There were no differences in rates of serious infections or malignancies, and there were no cases of tuberculosis or demyelinating disease, he said.

Dr. Emery disclosed that he has received consulting fees from Amgen Inc. and Wyeth. ■