Combo Regimen Increases RA Remission Rates

BY MITCHEL L. ZOLER

COPENHAGEN — Ongoing treatment of rheumatoid arthritis patients with a combination of etanercept plus methotrexate led to better outcomes during 2 years of therapy than did methotrexate alone, according to findings from an extended follow-up of the COMET trial presented at the annual European Congress of Rheumatology.

"The combination of etanercept and methotrexate produces a high rate of remission that is sustained over 2 years without increased toxicity," said Dr. Paul Emery, lead investigator for the COMET (Combination of Methotrexate and Etanercept in Active Early Rheumatoid Arthritis) trial.

The 2-year data also show that delaying the start of combination therapy in patients with active, early, moderate to severe rheumatoid arthritis (RA) by treating them with methotrexate alone for a year and then switching to the combined regimen did not work as well as starting the combined treatment at once. "The best time to start etanercept is as soon as possible for the majority of patients," said Dr. Emery, the Arthritis Research Campaign Professor of Rheumatology at the University of Leeds (England).

The COMET trial enrolled patients aged 18 years or older who had adult-onset RA diagnosed for at least 3 months but not more than 2 years. Their DAS28 (disease activity score 28) was 3.2 or higher, and they had either a Westergren erythrocyte sedimentation rate of at least 28 mm/hour or a C-reactive protein level of at least 20 mg/L. Patients had not previously been treated with etanercept, another tumor necrosis factor antagonist, or methotrexate.

Patients were randomized to treatment with either 50-mg etanercept by subcutaneous injection once weekly or placebo. All patients received oral methotrexate, starting at 7.5 mg once per week and increasing if needed up to 20 mg/week.

The study's two primary outcomes were the percentage of patients achieving remission after 52 weeks of treatment (a DAS28 score of less than 2.6), and their radiographic nonprogression. In all, 528 patients (265 on combined treatment and 263 on methotrexate only) were evaluable for the primary end points.

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After 1 year, 50% of patients in the combined-treatment group and 28% in the methotrexate-only group achieved a DAS28 remission, a statistically significant difference. The rate of radiographic nonprogression was 80% with combined treatment and 59% with methotrexate only, also a statistically significant difference (Lancet 2008;372:375-82).

For the year-2 analysis, 222 patients who completed the first year on etanercept plus methotrexate were randomized either to continue the combination or to switch to etanercept alone. From the control arm, 189 patients who completed 1 year on methotrexate monotherapy were either continued on methotrexate only or begun on methotrexate plus etanercept.

At the end of year 2, the remission rate in the nonresponders imputation analysis was 46% in patients who were on the combined regimen for the entire 2 years and 24% in patients who received methotrexate alone throughout. The remission rates were between these two rates for patients who were switched from both drugs to etanercept alone after 1 year (a 38% remission rate), and for those switched from methotrexate only to both drugs after 1 year (a 37% remission rate). Radiographic nonprogression was also greatest (90%) in the patients who got both drugs for 2 years, and was lowest (68%) in those on methotrexate only for 2 years, Dr. Emery reported.

The trial was sponsored by Wyeth, which markets etanercept in partnership with Amgen Inc. Dr. Emery has received research grants from and has served as a consultant to Wyeth. ■