Adalimumab Plus Methotrexate Versus Methotrexate Monotherapy in Early RA

Written by Toni Rizzo

Jacqueline Detert, MD, Charité Universitätsmedizin Berlin, Berlin, Germany, presented results from the High Induction Therapy with Anti-Rheumatic Drugs study [HIT HARD], which compared treatment with adalimumab plus methotrexate with methotrexate monotherapy in disease-modifying antirheumatic drug (DMARD)-naïve patients with active early rheumatoid arthritis (RA). The central question of the study was whether or not early induction therapy with a subsequent step-down strategy leads to long-term clinical effect in patients with RA.

Patients in this multicenter trial were randomized to treatment with subcutaneous (SC) adalimumab plus methotrexate (n=87) versus methotrexate alone (n=85) for the first 24 weeks. After Week 24, both groups received methotrexate monotherapy up to Week 48. The primary endpoint was DAS28 at 48 weeks. Secondary endpoints included radiological changes in the hands and feet (modified Sharp score and Ratingen score); American College of Rheumatology (ACR) 20/5/70; WHO/ILAR core set variables; safety; and changes in glucocorticoid, NSAID, and COX-2 inhibitor dosages.

Baseline characteristics were similar in both treatment groups. At baseline, the patients had a mean disease duration of 1.7 months, mean DAS28 of 6.2, mean HAQ of 1.4, and Sharp-van der Heijde total score of 8.8. A total of 76 patients in the induction group and 57 patients in the placebo group completed 48 weeks of treatment.

The combination group (induction group) had significantly decreased Disease Activity Score (DAS) 28 versus the placebo group at Weeks 8 (3.2 vs 4.5), 16 (3.0 vs 3.9), and 24 (3.0 vs 3.6; $p<0.05$ for all), but there was no significant difference between the groups during the methotrexate monotherapy phase (Weeks 32 to 48). Likewise, significantly more patients in the induction versus the placebo group achieved remission (DAS28 <2.6) during the first 24 weeks, but the difference narrowed during Weeks 32 to 48. The ACR response rates at Week 24 for the induction versus the placebo group were: ACR20 (79% vs 68%; p=NS), ACR50 (64% vs 49%; $p<0.05$), and ACR70 (48% vs 27%; $p<0.05$). The ACR response rates at Week 48 were not significantly different between the induction and the placebo groups: ACR20 (66% vs 75%), ACR50 (53% vs 51%), and ACR70 (40% vs 34%). The mean HAQ values were significantly improved in the induction versus placebo group at Weeks 8 (0.6 vs 1.0; $p<0.001$), 16 (0.6 vs 0.8; $p<0.001$), and 24 (0.5 vs 0.7; $p<0.05$) but were not significantly different at Weeks 32, 40, or 48.

Radiographic progression was significantly reduced in the induction group compared with the placebo group (total Sharp-van der Heijde score adalimumab 2.6 vs methotrexate 6.4; p=0.03) at Week 48. No new safety signals were detected.

Combination therapy with adalimumab and methotrexate was significantly superior to methotrexate alone during the initial treatment phase of 24 weeks. Reduced radiographic progression was observed at Week 48, indicating a sustained effect of combination treatment. However, reduction in disease activity, the primary endpoint, was not sustained through 48 weeks. The numerical increase in the clinical outcome parameters of the adalimumab-plus-methotrexate group from Week 40 onwards may reflect the loss of response after removal of adalimumab.

Results From the ESPOIR Cohort Study

Written by Toni Rizzo

Laure Gossec, MD, PhD, Paris Descartes University, Paris, France, presented results from the French Early Arthritis (ESPOIR) cohort study. Investigators analyzed patients who were in remission to determine if a patient's global status assessment and fatigue rating during the first year of early arthritis play a significant role in predicting structural progression over 3 years.

ESPOIR is an observational study of patients with early arthritis who had no prior disease-modifying antirheumatic drug (DMARD) therapy. Early arthritis was defined as having at least 2 swollen joints for <6 months. The outcome was change in total Sharp-van der Heijde score (SHS) from baseline to 3 years, adjusted for baseline radiographic score. Predictive variables included definitions of remission at 6 and 12 months, swollen and tender joints, C-reactive protein (CRP), global assessment, and fatigue rating (means of 6- and 12-month values). Remission definitions that were used were the ACR/EULAR Boolean remission (tender and swollen joint counts ≤1, CRP ≤1 mg/dL, and patient global ≤1/10), no-patient-reported outcome (PRO)