One-Year Results From the AMPLE Study

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To date, no randomized, controlled studies have directly compared the safety and efficacy of different biologic disease-modifying antirheumatic drugs in rheumatoid arthritis (RA). Michael Schiff, MD, University of Colorado, Denver, Colorado, USA, presented the 1-year results of a head-to-head study that compared the efficacy and safety of subcutaneous abatacept versus adalimumab, both with background methotrexate. The results demonstrated comparable efficacy (by noninferiority analysis) and similar kinetics of response and inhibition of radiographic progression at 1 year. Safety was generally similar, with fewer discontinuations and significantly fewer injection-site reactions observed with abatacept.

The Abatacept Versus Adalimumab Comparison in Biologic-Naïve RA Subjects With Background Methotrexate study [AMPLE; NCT00929864] is a Phase 3b, randomized, investigator-blinded, noninferiority study of 24-months' duration with a 12-month efficacy primary endpoint. Biologic-naïve patients with active RA (Disease Activity Score [DAS] 28-C-reactive protein [CRP] ≥3.2) of ≤5 years and inadequate response to methotrexate were randomized to either 125 mg subcutaneous abatacept (without an intravenous load; n=318) weekly or 40 mg subcutaneous adalimumab biweekly (n=328). All subjects received a stable dose of methotrexate. The primary endpoint was noninferiority by ACR20 response at 12 months with a noninferiority margin of 12%. Key secondary endpoints included the frequency of injection-site reactions, radiographic nonprogression (van der Heijde-modified total Sharp score [mTSS] method), safety, and retention.

The study comprised 646 subjects (mean age 51 years, mostly caucasian women, mean disease duration ~1.8 years). Subjects in this study had active disease; mean DAS28-CRP of 5.5; tender joint count of ~25, swollen joint count of ~16; and mean Health Assessment Questionnaire Disability Index (HAQ-DI) of 1.5. At 1 year, 82% of subjects in the adalimumab groups and 86.2% of patients in the abatacept group remained in the study.

At 1 year, on intent-to-treat analysis, the proportion of patients who achieved an ACR20 response was not significantly different: 64.8% in the abatacept group and 63.4% in the adalimumab group (estimated difference, 1.8; 95% CI for difference, -5.6 to 9.2). These results were confirmed by the per-protocol analysis. The kinetics of the response did not differ for the ACR20, ACR50, or ACR70 responses. The efficacy and kinetics of response, based on mean DAS28-CRP score, were also similar. At 1 year, 59.3% of abatacept and 61.4% of adalimumab subjects had achieved a DAS28-CRP of ≤3.2. DAS28-CRP remission (<2.6) was achieved by 43.3% of abatacept-treated patients and 41.9% of adalimumab-treated subjects. Radiographic nonprogression rates were comparable, and the mean changes in mTSS were 0.58 versus 0.38 for abatacept versus adalimumab, respectively.

The rates of adverse events (AEs), serious AEs (SAEs), serious infections, and malignancies were comparable. There were more subjects with autoimmune AEs (10 vs 4) in the abatacept arm; none was an SAE. There were fewer discontinuations, including those because of AEs (3.5% vs 6.1%) and those because of SAEs (1.3% vs 3.0%), in the abatacept arm. The most common infections were pneumonia (3 subjects in the abatacept arm and 2 in the adalimumab arm), urinary tract infections (3 subjects who were taking abatacept), and bacterial arthritis (3 subjects in the adalimumab arm). Injection-site reactions occurred in 3.8% of abatacept versus 9.1% of adalimumab subjects (difference, -5.37; 95% CI for difference, -9.13 to -1.62; p=0.006).

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