Tocilizumab Is Beneficial in Moderate to Severe RA

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BARCELONA — In a multicenter double-blind study, treatment with the interleukin-6 signaling blocker tocilizumab not only significantly reduced disease activity among patients with rheumatoid arthritis but also improved physical function, fatigue, and quality of life.

A total of 622 patients with moderate to severe rheumatoid arthritis (RA) were randomized to receive intravenous tocilizumab in doses of 4 mg/kg or 8 mg/kg every 4 weeks or placebo. They also received background methotrexate in doses of 10-25 mg/week and corticosteroids in doses of 10 mg/day or less, according to Dr. Rieke H.E. Alten of the Schlosspark Klinik, Berlin.

The patients’ mean age was 51 years, and more than half were women. Their mean disease duration was 7.5 years, and they had taken a mean of 1.5 disease-modifying antirheumatic drugs before undertaking the experimental regimen. All of them had swollen joint counts of six or more and tender joint counts of at least eight.

By week 24, a significantly greater proportion of patients treated with tocilizumab achieved an American College of Rheumatology (ACR) 20 response than did those who received placebo. In patients in the low-dose tocilizumab group, 13.5% achieved this level of response, as did 27.5% of those in the high-dose group. In those receiving placebo, 0.8% reached an ACR20 level of response, Dr. Alten reported in a poster session at the annual European Congress of Rheumatology.

Tocilizumab treatment also resulted in a marked increase in the proportion of patients who achieved moderate or good response according to the criteria of the European League Against Rheumatism. A total of 61.9% and 79.5% of patients in the low- and high-dose groups, respectively, had moderate or good responses.

On the Health Assessment Questionnaire...
Disability Index (HAQ-DI), clinically relevant improvements were seen in patients in both tocilizumab groups, starting at week 4, and with greater mean reductions than the protocol-defined minimally clinically relevant difference of 0.25.

In patients in the tocilizumab 4-mg- and 8-mg/kg groups, 64.8% and 63.1%, respectively, had a >20% or greater improvement in HAQ-DI, compared with 47.5% of the placebo patients.

All treatment groups showed improvements in the physical and mental components of the Short Form–36 Health Survey. Functional Assessment of Chronic Illness Therapy (FACT–IT)–Fatigue Scale scores also improved in all treatment groups, but greater mean changes were consistently observed for patients in the tocilizumab groups, he wrote. Moreover, the FACT fatigue score increased by a clinically meaningful four points or more from baseline by week 4 in both tocilizumab groups.

RA is associated with functional disability, limitation of daily activities, and decreased quality of life. Fatigue is a particular problem, with more than 40% of patients reporting clinically important levels of fatigue, Dr. Alten noted.

The greater the proportion of patients reporting IL-6 in RA lies in observations that this cytokine appears to play a role in the damage to periarticular bone and cartilage. It also activates T cells, B cells, and macrophages and is a central mediator of the hepatic acute phase response (Lancet 2007; doi:10.1016/S0140-6736(07)6784-4).

The study was sponsored by Hoffmann-La Roche Inc.

Long-Term Steroids in RA May Cut Function

Barcelona — Rheumatoid arthritis patients who use corticosteroids frequently over the long term can maintain a low disease activity state but suffer derangement of their functional capacity, Dr. Eiichi Tanaka reported at a poster session at the annual European Congress of Rheumatology.

A low disease activity state caused by corticosteroid use may not represent a ‘true’ low disease activity state,” noted Dr. Tanaka of Tokyo Women’s Medical University, and his associates.

The investigators followed 224 RA patients with a low disease activity state during 2000-2005.

The patients had a mean age of 56 years and a mean disease duration of about 8 years, and were enrolled in the study for at least 3 years. Every 6 months, the investigators collected measurements on the Disease Activity Score–28 (DAS-28) and Japanese version of the Health Assessment Questionnaire (J-HAQ).

DAS-28 scores did not change substantially over the course of the study. Of 135 patients who never used corticosteroids, 33 who used steroids an average of less than 9 months per year, and 56 who took steroids an average of more than 9 months per year.

No patient had a DAS-28 greater than 3.2 at each assessment.

But long-term functional capacity, as measured by the J-HAQ, declined in the heavy corticosteroid users, improved slightly among moderate corticosteroid users, and improved the most in patients who did not use corticosteroids.

The use of corticosteroids was the most significant factor contributing to the final J-HAQ score, after the adjustment of a multiple linear regression analysis for age, gender, disease duration, initial J-HAQ score, and seasonal effects.

A little more than 90% of the patients in each group used disease-modifying anti-rheumatic drugs during the study.

Along with the achievement of a low disease activity state, long-term efficacy, long-term functional prognosis, and the quality of remission also need to be considered in the strict control of RA activity,” Dr. Tanaka and his colleagues concluded.