Infliximab Boosts Psoriatic Spondyloarthropathy Rx

BY KERRI WACHTER
Senior Writer

BUDAPEST, HUNGARY — Infliximab, in combination with methotrexate, shows promising results in reducing the severity of psoriatic spondyloarthropathy, based on the results of a 2-year open-label study presented at the 4th International Congress on Autoimmunity.

Most of the 16 patients in the study showed improvement on several measures, according to Juan J. Scali, M.D., of Durand Hospital, Buenos Aires.

The patients in the study—nine men and seven women with a mean age of 38 years—had severe manifestations of the disease, little or no response to methotrexate, and a mean disease duration of 16 years. Seven patients were positive for HLA-B27, which is associated with ankylosing spondylitis.

Patients were given 5 mg of infliximab (Remicade) per kg of body weight as an intravenous infusion at baseline, at 2 and 6 weeks, and then once a month. They were continued on methotrexate 15 mg/wk.

Patients were evaluated using the psoriatic arthritis response criteria (PsARC) and the American College of Rheumatology (ACR) response criteria (20, 50, and 70). With PsARC, a patient must show improvement in two of the four measures—at least 30% reduction of tender joint count, at least a 30% reduction of swollen joint count, a decrease of at least 1 point on the physician global assessment, and a decrease of at least 1 point on the patient global assessment on a visual analog scale—to be a considered a responder. When the ACR response criteria are used, the patient must show a 20%, 50%, or 70% improvement in tender joint count, swollen joint count, and three of five other measures—patient assessment, physician assessment, erythrocyte sedimentation rate, pain scale, or functional questionnaire.

At the end of 24 months, 88%, 56%, and 31% of patients responded to treatment using the ACR 20, 50, and 70. With PsARC, 88% of patients had improvement at the end of the first year and 74% at the end of the second year.

Psoriasis activity was also measured using the Psoriasis Area and Severity Index (PASI). Patients were considered to have active disease with a PASI score of 16 or greater. At 1 year, 90% of patients showed an improvement in PASI scores, which dropped to 80% at 2 years. Also, 70% of patients had a favorable opinion of their response at the end of 2 years. Infliximab had good safety overall; no patients had allergic reactions or adverse events, he said.

Dr. Scali noted that the best results were seen at around 20 months. He recommended 6-12 months of infliximab therapy, followed by methotrexate alone. ■

Combination Demonstrates Promise in Psoriatic Arthritis

BY BETSY BATES
Los Angeles Bureau

PARIS — Combining agents with complementary mechanisms and pharmacokinetic profiles may hold promise even for patients with severe psoriatic arthritis who have been failed by every other form of therapy.

German researchers used that approach, combining leflunomide (Arava) and etanercept (Enbrel) in two severely affected patients, with excellent results.

Jochen Schmitt, M.D., and Gottfried Wozel, M.D., of the department of dermatology at University Hospital Carl Gustav Carus of Dresden University of Technology presented their findings at the European Congress on Psoriasis 2004.

Confronted with patients who had severe swollen and tender joints, extensive psoriatic plaques, and profoundly affected quality of life and for whom an array of therapeutic options had failed, they decided to combine leflunomide and etanercept.

"The rationale of the combination is based on the predominant role of T cells and proinflammatory cytokines such as TNF-α in the pathogenesis of psoriasis," they noted in a poster presentation.

"The active metabolite of leflunomide interferes with T-cell proliferation by inhibition of dihydroorotate dehydrogenase, a key enzyme of pyrimidine de novo synthesis," and etanercept, a TNF-α receptor, P75 fusion protein, blocks biologic activity to TNF-α, according to the investigators.

Leflunomide was prescribed at an initial dosage of 100 mg for 3 days, then tapered to 20 mg and then to 10 mg. Patients received etanercept in 25-mg, twice-weekly subcutaneous injections.

The response was dramatic during the course of the 8-week study period and a follow-up period that extended 20 more weeks. The first patient went from 32 swollen and 30 tender joints, a Psoriasis Area and Severity Index (PASI) score of 52.6; and a Dermatology Life Quality Assessment score (DLQI) of 19, to 9 swollen and 8 tender joints, a PASI score of 1.8, and a DLQI score of 3.

The second patient was less severely affected at baseline but exhibited a complete remission. Specifically, she went from nine swollen and nine tender joints to zero; her PASI score dropped from 17.6 to 0, and her DLQI score declined from 3 to 0.

The researchers commented on the two drugs' complementary pharmacokinetic profiles.

"Leflunomide's active metabolite exhibits an extremely long half-life in vivo. Etanercept features an early onset of efficacy. Thus, in severe psoriasis, it might be reasonable to use leflunomide as a basic agent and to add etanercept when a relapse occurs," Dr. Schmitt said. ■

Abatacept Plus MTX Effective, Safe in RA

BY NANCY WALSH
New York Bureau

SAN ANTONIO — Adding the selective costimulatory modulator abatacept to methotrexate in patients with rheumatoid arthritis who do not respond adequately to methotrexate alone resulted in "robust clinical efficacy" that persisted for 2 years, according to the findings of an extension study.

Among patients who completed 2 years of treatment, response rates were similar at 2 years to what they were at 1 year, Joel M. Kremer, M.D., said in a poster session at the annual meeting of the American College of Rheumatology. (See chart.)

In the initial double-blind phase of the trial, 115 participants whose mean age was 55.6 years and whose mean disease duration was 10 years were randomized to receive intravenous abatacept (10 mg/kg monthly) plus methotrexate in a stable dose of 10 to 30 mg/week for 1 year.

Those who completed the yearlong blinded phase were eligible to enroll in the long-term open trial, which used a fixed dose of abatacept (about 10 mg/kg) along with methotrexate.

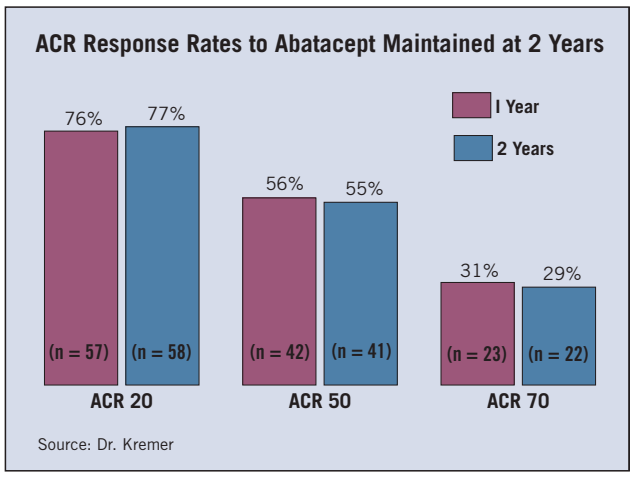
A total of 84 patients entered the open phase and 75 completed the full 2 years. High rates of retention in the trial, along with improved ACR scores, demonstrated consistent and sustained clinical efficacy, said Dr. Kremer, director of research at the Center for Rheumatology, Albany, N.Y.

In addition to the standard American College of Rheumatology (ACR) 20, 50, and 70 responses, ACR 90 responses were assessed. This score was achieved by more than 13% of patients at year 1 and almost 15% at year 2.

During the double-blind phase of the study, the most common adverse events were nasopharyngitis, headache, nausea, and cough. There were no new emerging safety issues during the long-term extension phase, he said.

Abatacept is the first in a new class of agents that inhibit the full activation of T cells. It blocks the engagement of the costimulatory molecule CD28, resulting in the inhibition of cytokines that activate inflammatory cells.

Dr. Kremer disclosed that he receives research grants and consulting fees from multiple sponsors, including Bristol-Myers Squibb Co., the manufacturer of abatacept. ■



Psoriatic Arthritis Indication for Infliximab Under FDA Review

The U.S. Food and Drug Administration has accepted Centocor Inc.'s application to approve infliximab (Remicade) for the treatment of psoriatic arthritis.

Already approved for use in rheumatoid arthritis and Crohn's disease in North America, the European Union, and Japan, infliximab was recently approved for use in psoriatic arthritis by the European Commission.

Centocor, a wholly owned subsidiary of Johnson & Johnson, based its application on two double-blind, placebo-controlled studies involving a total of 304 patients with psoriatic arthritis. In one study, 65% of the patients on infliximab (5 mg/kg) achieved at least a 20% improvement, according to American College of Rheumatology (ACR20) criteria at week 16.

In the second study, some patients taking 5 mg/kg of infliximab began showing improvement as early as week 2. By week 14, 58% of the patients taking infliximab and only 11% of the patients taking placebo achieved ACR20 improvement. The Psoriasis Area and Severity Index score improved by 75% in 63.9% of the infliximab patients and only 2.3% of the placebo patients. Both differences were statistically significant.

Patients with psoriatic arthritis tolerated infliximab well in these studies, with an elevation in liver function tests being the most common abnormality associated with the drug, which inhibits tumor necrosis factor alpha. Investigators noted no deaths, cases of tuberculosis, or other opportunistic infections among the patients taking infliximab in these studies.

—Robert Finn