

Etanercept Significantly Helped Heel Enthesitis

BY MITCHEL L. ZOLER

COPENHAGEN — Treatment with etanercept produced significant clinical improvement in heel enthesitis associated with spondyloarthritis, according to Dr. Maxime Dougados.

“This study demonstrates the efficacy of etanercept in [enthesopathy] related to spondyloarthritis, whatever the underlying disease” including ankylosing spondylitis or psoriatic arthritis, said Prof. Dougados, director of the research center in the department of rheumatology at Hôpital Cochin, Paris.

This 12-week, controlled study with 24 patients is the first prospective, placebo-controlled trial of a treatment for enthesopathy related to spondyloarthritis, added Prof. Dougados, who presented the findings at the annual European Congress of Rheumatology.

The benefit on symptoms from 12 weeks of etanercept treatment vs. placebo was clinically as well as statistically significant.

Patients on etanercept experienced substantial improvements from baseline on a variety of measures, including their global assessment (the primary outcome), heel pain, and WOMAC (Western Ontario and McMaster Universities) osteoarthritis index functional subscale score.

“Despite the small sample size [a total of 24 patients], the results seen not only in the primary variable but also in all the secondary variables are strongly in favor” of etanercept’s efficacy for heel enthesitis, Prof. Dougados said in an interview with RHEUMATOLOGY NEWS. “I hope the trial will be replicated by evaluating the other TNF [tumor necrosis factor] blockers.”

Heel enthesitis is common in



The infection risk seen with all anti-TNF agents is outweighed by the benefit of preventing disability.

DR. DOUGADOS

patients with spondyloarthritis regardless of the underlying cause, occurring in 40%-50% of these patients, and can be disabling, according to Dr. Dougados.

Although etanercept and other TNF-blocking drugs have proved to be effective for reducing many of the main clinical manifestations of spondyloarthritis (such as peripheral arthritis, axial symptoms, and psoriatic skin lesions), the impact of these treatments on heel enthesitis was not known prior to this investigation.

The study, which was done at six hospitals in France, Germany, and the Netherlands, en-

rolled patients older than 18 years who had spondyloarthritis and related heel enthesitis that was refractory to standard treatment with NSAIDs and local injections of corticosteroids.

The AS patients’ heel enthesitis was documented by their inferior and/or posterior heel pain and by an MRI scan showing bone marrow edema in the calcaneus adjacent to the insertion of either the Achilles tendon or plantar fascia. The average age of enrolled patients was 37 years.

In all, 12 patients began a 12-week course of standard etanercept treatment, and the other 12 received placebo.

During the study, five patients stopped treatment (four in the placebo group because of lack of efficacy, and one in the etanercept group because of a severe infection in the form of foot cellulitis that required hospitalization).

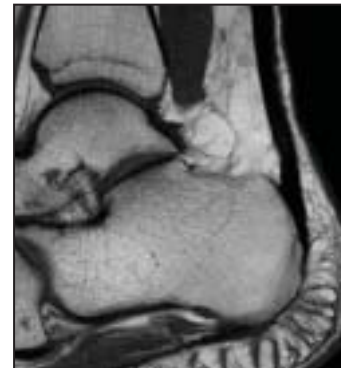
At the end of the treatment period, the average change in patients’ global score on a visual analog scale of 0-100 was a reduction of 29 points from a baseline average of 70 in the etanercept-treated patients, compared with a reduction of 11 points in the placebo-treated patients.

After 2 weeks, the patients receiving etanercept began to show improvement in global score and other measurements.

By the end of 8 weeks, those differences between active treatment and placebo reached a sta-



On STIR MR images (above), note the areas of high signal in the inferior calcaneus that correspond to bone marrow edema.



Sagittal T1 MR images of the same heels show thickening with heterogeneous high signal of the plantar fascia in a patient with heel pain due to AS-related enthesitis.

tistically significant difference, compared with placebo, reported Prof. Dougados, who is also professor of rheumatology at René Descartes University in Paris.

During the study, five patients on etanercept and three on placebo had infections, primarily upper respiratory. All resolved once treatment was complete.

The well-documented risk for infection from treatment with etanercept or other TNF

blockers must be balanced against the risk from conventional treatments for enthesopathy, as well as the risk that enthesitis poses for causing disability in young patients, Dr. Dougados noted.

The study was sponsored by Wyeth Pharmaceuticals, the company that markets the drug etanercept.

Prof. Dougados has been a consultant to Wyeth and to several other drug companies. ■

Methotrexate/Tocilizumab Combo Offers New Option for RA

BY DIANA MAHONEY

COPENHAGEN — The addition of tocilizumab to methotrexate therapy is a promising new option for rheumatoid arthritis patients who do not fully respond to treatment with the disease-modifying antirheumatic drug alone, Dr. Joel M. Kremer said at the annual European Congress on Rheumatology.

Dr. Kremer, director of research at the Center for Rheumatology LLC in Albany, N.Y., presented 1-year data from the international LITHE (Tocilizumab Safety and the Prevention of Structural Joint Damage) study showing that the anti-interleukin-6 monoclonal antibody inhibits structural joint damage and improves physical function and clinical disease activity, compared with methotrexate alone.

The randomized, double-blind, placebo-controlled LITHE study, which was sponsored by Roche, enrolled 1,196 patients with moderate to severe rheumatoid arthritis who had an inadequate response to methotrexate. Patients were randomized to receive a 4-mg/kg or 8-mg/kg infusion of tocilizumab (Actemra) every 4 weeks in combination with stable doses of methotrexate or methotrexate/placebo. The study’s primary end points included ACR 20 response at 24 weeks and change from baseline in Genant-modified Total Sharp

Score (GmTSS) and physical function at 52 weeks, measured by area under the curve (AUC) of change from baseline in the Health Assessment Questionnaire Disability Index (HAQ-DI), Dr. Kremer explained.

At 24 weeks, ACR 20 response was achieved by 56% and 51%, respectively, in the tocilizumab 8-mg and 4-mg combination therapy groups, compared with 27% of the methotrexate-only group, Dr. Kremer said, noting that significantly more patients in both combination therapy groups achieved ARC 20/50/70 responses at week 52.

Also at 52 weeks, there were significantly more patients in the combination therapy groups without radiographic progression from baseline, compared with the methotrexate-only group. Total GmTSS change from baseline for the tocilizumab (8 mg)/methotrexate, the tocilizumab (4 mg)/methotrexate, and the methotrexate-only groups were 0.29, 0.34 and 1.13, respectively. The respective percentages of patients achieving no progression in GmTSS were 85%, 81%, and 67%, Dr. Kremer said. The HAQ-DI AUC changes from baseline adjusted mean scores were -144.1, -128.4 and -58.1, respectively. At 24 and 52 weeks, the DAS28 (Disease Activity Score based on 28 joints) clinical remission scores were significantly greater in the combination therapy groups, compared with the methotrexate-only group. In both combination therapy groups,

the DAS28 remission rate increased from week 24 to week 52, indicating an increasing magnitude of clinical benefit over time, he said.

“Tocilizumab represents a new approach to treating severe arthritis, but as always, the decision to use a particular biologic agent is not cast in stone” Dr. Kremer said in an interview. “There will always be patients in any busy practice who have tried and failed the multiple agents previously available.” In these patients, he said, “trying a new mechanism of action, while watching carefully for the emergence of side effects, is reasonable.”

In particular, patients must be monitored for abnormalities in transaminase enzymes, which would require an adjustment in the dose of either medication, Dr. Kremer said. In the event of significant increases in lipid levels in a patient with underlying risk factors for cardiovascular disease, strong consideration should be given to the initiation of a statin agent, he said.

Dr. Kremer, who is also the founder and president of CORRONA (Consortium of Rheumatology Researchers of North America), disclosed that he has received grants for clinical research from—and has served as a consultant for—Abbott Laboratories, Amgen Inc., Bristol-Myers Squibb Co., Centocor Inc., Genentech Inc., and Roche. ■