Abatacept Slows Rheumatoid Arthritis Damage

BY NANCY WALSH
New York Bureau

AMSTERDAM — Two-year abatacept treatment of rheumatoid arthritis resulted in significant inhibition of radiographic damage in the long-term, open-label extension phase of the Abatacept in Inadequate Responders to Methotrexate trial, Dr. Harry K. Genant reported at the annual European Congress of Rheumatology.

Of the patients who completed the initial 1-year double-blind phase of the Abatacept in Inadequate responders to Methotrexate (AIM) trial, 539 were included in the extension phase. The patients received abatacept in doses of approximately 10 mg/kg every 4 weeks, plus a stable dose of methotrexate. Joint changes were evaluated as mean changes from baselines on the composite Genant-modified Sharp score, which rates the progression of joint erosions and joint space narrowing.

The mean change in total Sharp score from baseline in patients randomized to the abatacept group at year 1 was 1.07.

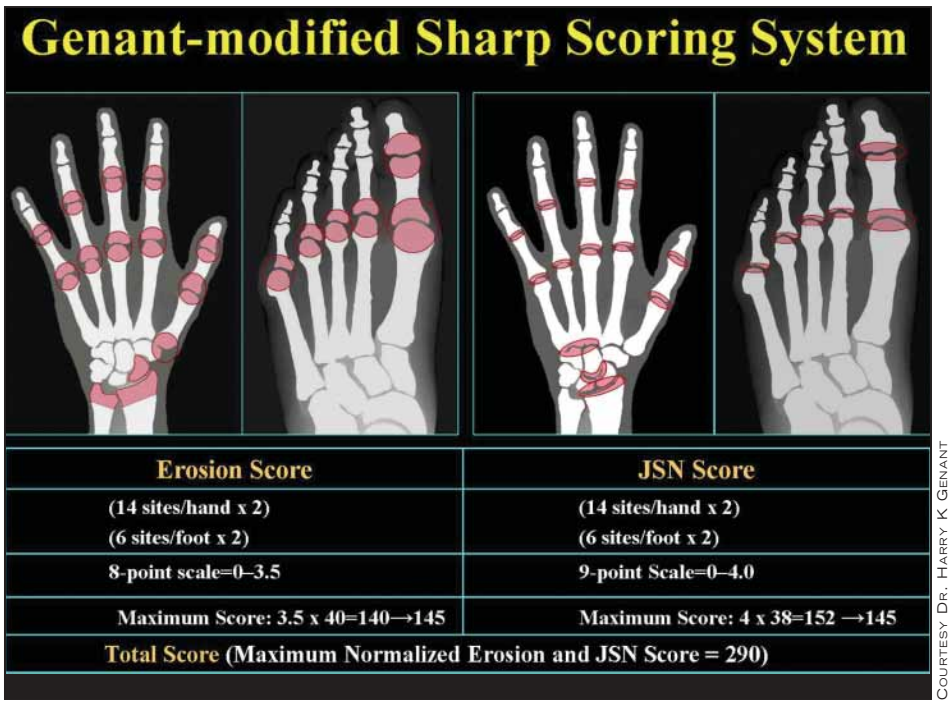
By year 2, the mean change was 1.55, according to Dr. Genant, who is professor emeritus, University of California, San Francisco, and chairman emeritus, Synarc Inc., San Francisco.

"Among these patients, there was less radiographic progression during the second year than during the first year. In fact, disease progression during year 2 was about 57% less than during year 1, representing an acceleration of the effectiveness of the drug," Dr. Genant said at a press briefing unveiling the AIM trial results.

RA progression during year 2 was less than during year 1, suggesting an acceleration of the drug's effectiveness.

DR. GENANT

Among those patients who initially were randomized to the placebo group, the mean change from baseline in total Sharp score was 2.40 at year 1. At year 2, after having been switched to active treatment, these patients' mean Sharp score was 3.17.



COURTESY DR. HARRY K. GENANT

The change in mean score at year 2, compared with that at year 1, was 0.46 in the abatacept group and 0.75 in the placebo group, Dr. Genant reported at the meeting.

Measures of clinical efficacy also showed durable responses during the second year of therapy, Dr. Joel M. Kremer reported in a poster session at the meeting, sponsored by the European League Against Rheumatism.

At year 1, 82% of patients who had received abatacept plus methotrexate achieved American College of Rheumatology (ACR) 20 responses, 54% achieved ACR 50 responses, and 32% achieved ACR 70 responses. The corresponding numbers at year 2 were 80%, 56%, and 34%, according to Dr. Kremer of Albany (N.Y.) Medical College.

By the completion of the long-term extension phase of the trial, participants who initially had received placebo but had been receiving abatacept for 1 year had similar clinical responses to those who had been receiving the active treatment for 2 years, with 78% achieving ACR 20 responses, and 58% and 32% achieving ACR 50 and 70 responses, respectively.

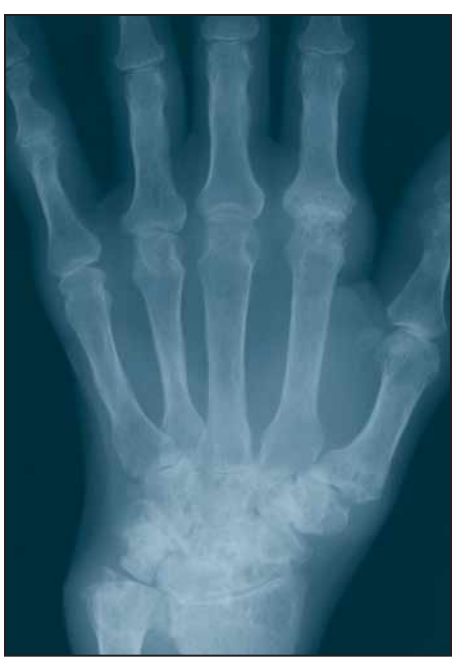
Remission, defined as a score of less than 2.6 on the Disease Activity Score (DAS 28), was reached by 25.4% of patients in the abatacept group at year 1, compared with 2.5% of those in the placebo group.

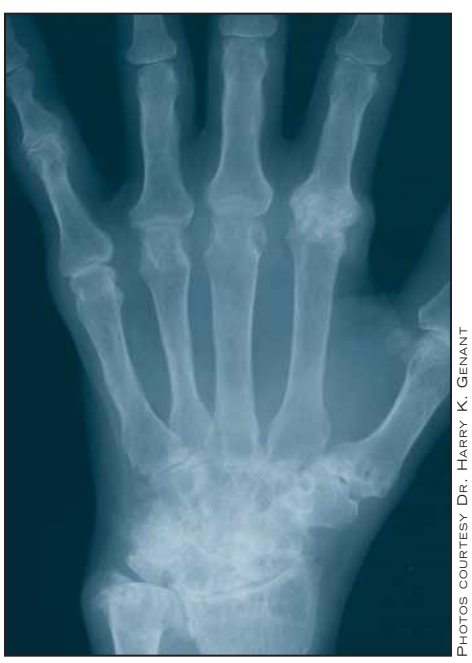
By the completion of the second year of the investigation, rates of remission were similar in the two groups, regardless of initial randomization, at 30.9% and 32.6% in the active treatment and placebo groups, respectively.

The AIM investigation initially included 652 patients from 116 centers worldwide. The results of the double-blind phase of the trial were the basis for regulatory approval of the drug in the United States, which was granted in December 2005.

Abatacept (Orencia) is a selective modulator of the CD80/CD86:CD28 costimulatory signal that is required for T-cell activation.

Dr. Genant has received consulting fees from Synarc, and Dr. Kremer has received research grants and consulting fees from Bristol-Myers Squibb. ■





PHOTOS COURTESY DR. HARRY K. GENANT

An abatacept-treated patient's left hand is shown on radiography at baseline (left). The follow-up radiograph at 2 years shows moderate joint damage indicating stable, nonprogressive disease with the biologic.