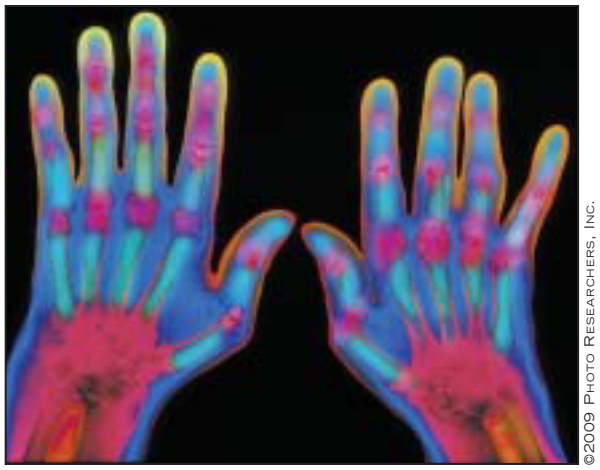

Color-enhanced X-ray of hands showing severe rheumatoid arthritis. Swelling and bone deformation (pink) is seen in finger joints between metacarpal and phalanges bones, and between the phalanges bones themselves. Most joints are ragged due to bone erosion, with the thumbs also affected.

Early RA May Benefit From Prompt Infliximab

BY SALLY KOCH KUBETIN

The prompt addition of infliximab to methotrexate in patients with early rheumatoid arthritis who did not respond to brief monotherapy produced clinically superior results at 1 year, compared with adjuvant therapy with conventional disease-modifying antirheumatic drugs, according to the ongoing SWEFOT trial.

In addition, treating all patients with methotrexate monotherapy for 3-4 months screens out a sizeable proportion who would have been overtreated with the aggressive combination of methotrexate and infliximab, thus sparing them the increased risk for side effects as well

as the higher costs of therapy with a tumor necrosis factor inhibitor, according to Dr. Ronald F. van Vollenhoven, a rheumatologist at the Karolinska University Hospital in Stockholm, and his associates.

Some patients may lose important ground to RA during the first 3-4 months of treatment with methotrexate monotherapy. However, findings from a review of clinical trials with anti-TNF agents suggest that only negligible gains are achieved by immediate initiation of such agents, the investigators noted (Lancet 2009;374:459-66).

The trial conducted by Dr. van Vollenhoven and his associates involved 487 patients with rheumatoid arthritis of duration less than 1 year who were treated at any of 15 rheumatology centers in Sweden between October 2002 and December 2005. All patients were treated with methotrexate monotherapy for 3-4 months at a dosage of up to 20 mg/week. At the end of baseline therapy, 145 patients had responded well to methotrexate monotherapy, defined as a DAS28 of no more than 3.2; those patients continued on methotrexate monotherapy.

Of the remaining patients, 128 patients were randomized to receive the addition of infliximab to methotrexate, and 130 patients received sulfasalazine, hydroxychloroquine, and methotrexate. Of the other patients who did not continue in the trial, 27 were intolerant to methotrexate, 9 developed another illness, and 48 cited a variety of other reasons for withdrawing from the study.

At the end of 12 months, 105 of the 128 patients in the infliximab-plus-methotrexate group and 89 of the 130 patients in the sulfasalazine/hydroxychloroquine-plus-methotrexate group remained on their allocated treatment.

Of those, 50 of 128 patients (39%) on infliximab plus methotrexate achieved the primary outcome of a good EULAR response, compared with 32 of 130 patients (25%) on sulfasalazine/hydroxychloroquine plus methotrexate. The differences between the two treatment groups became statistically significant over time. The differences were very small and not statistically significant at 3 months when patients were initially randomized, but they increased at 6 months ($P = .0988$) and again at 12 months ($P = .0160$).

More patients in the infliximab-plus-methotrexate group achieved secondary outcomes than did those on sulfasalazine/hydroxychloroquine plus methotrexate. Secondary outcomes were EULAR good to moderate response, ACR 20, ACR 50, and ACR 70.

The study's findings "suggest that the most important information to be gathered from clinical trials in rheumatoid arthritis is not necessarily comparisons of agents, but rather the strategy of tight control, aiming for remission," Dr. Tuulikki Sokka and Dr. Theodore Pincus stated in an editorial.

Patients with rheumatoid arthritis have substantially better clinical status now than did their peers 2-3 decades ago, they noted. However, most of the improved status cannot be attributed to the use of biologic agents; improved clinical status began in 2000, before the availability of biologic agents, according to Dr. Sokka, a rheumatologist at Jyväskylä (Finland) Central Hospital, and Dr. Pincus of New York University Medical Center (Lancet 2009;374:430-2).

In addition, trials showing the most impressive results do not always involve biologic agents. Finally, findings from earlier trials comparing methotrexate monotherapy to methotrexate used in combination with a biologic suggest that many patients have clinical and radiologic responses to methotrexate that are as favorable as those to biologic agents or combinations, Dr. Sokka and Dr. Pincus said.

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