Following Infliximab Halt, Persistent Response Noted

BY BRUCE JANCIN
Denver Bureau

AMSTERDAM — Early and aggressive therapy with infliximab and methotrexate may favorably alter the course of rheumatoid arthritis, according to new data from the Dutch BEST trial.

After 3 years of follow-up, 55% of the 120 BEST participants initially randomized to combined therapy with infliximab and methotrexate were able to wean off infliximab. They had discontinued infliximab a median of 26 weeks earlier, thereafter consistently maintaining a Disease Activity Score (DAS) of 2.4 or less, down from a mean baseline DAS of 4.3, Dr. Arie E. van der Bijl reported at the annual European Congress of Rheumatology.

After discontinuing infliximab, most of these patients remained on methotrexate maintenance monotherapy. Of particular note was the finding that 17 patients, or 14% of the original 120, were in clinical remission as defined by a DAS of 1.6 or less without any antirheumatic drugs.

BEST is a multicenter randomized trial comparing four different treatment strategies in 506 patients with early rheumatoid arthritis (RA). Although several audience members speculated that similarly favorable 3-year results might have been achieved with early methotrexate monotherapy, which is known to produce very good outcomes in a minority of RA patients, Dr. van der Bijl of Leiden University Medical Center, the Netherlands, was quick to correct them. Another of the four BEST study arms featured exactly that strategy, and the results in terms of rates of low disease activity or clinical remission weren't nearly as good as in the combined infliximab/methotrexate arm.

After 3 years of follow-up, 55% of the BEST participants were able to be weaned off infliximab.

DR. VAN DER BIJL

The new BEST results warrant cautious interpretation. Whether early infliximab plus methotrexate alters the course of RA must await longer-term follow-up, including radiologic evidence of prevention of progressive joint damage, he stressed.

BEST is supported by the Dutch government and the Dutch College of Health Insurance Companies. ■

Successful Stem Cell Transplants Offer Hope for Refractory Still's

BY NANCY WALSH
New York Bureau

GLASGOW, SCOTLAND — Successful stem cell transplantation in two patients with recalcitrant Still's disease suggests that this approach could offer a viable alternative for patients who do not respond to other therapies, according to Dr. Hanumantha V. Reddy.

Treatment typically includes nonsteroidal anti-inflammatory drugs, high-dose corticosteroids, and intravenous immunoglobulin. Disease-modifying antirheumatic drugs (DMARDs) are sometimes used, although they tend to be more beneficial for the articular symptoms than for the systemic abnormalities, noted Dr. Reddy in a poster session at the annual meeting of the British Society for Rheumatology.

In the first case, explained by Dr. Reddy, a 34-year-old woman had intermittent fever, rash, arthritis that was significantly erosive, leukocytosis, anemia, and elevated inflammatory markers. She was steroid dependent and had not responded to DMARDs or biologic therapies.

She underwent autologous stem cell transplantation in early 2003 and responded well, soon entering remission with normalization of her inflammatory markers. In 2004, she had a successful pregnancy, and she remains in remission, Dr. Reddy reported.

The second stem cell transplantation involved a 24-year-old woman who had been diagnosed with Still's disease at age 14 and had frequent flares but no significant joint damage. She too was steroid dependent and had not responded to traditional DMARDs, biologic therapies, or intravenous immunoglobulin, according to Dr. Reddy of the rheumatology department, Royal Liverpool University Hospital, England.

The patient underwent autologous stem cell transplantation. The posttransplant period was complicated by 3 months of persistent fever, presumed to be viral in origin. She also experienced two episodes of severe autoimmune hemolysis characterized by frank hematuria and the presence of Kidd group antibodies. She recovered well, however, and is currently in remission, Dr. Reddy reported.

Stem cell transplantation risks were seen in a series of 34 children with juvenile idiopathic arthritis who underwent the procedure. Although 53% of patients in this series responded well and experienced drug-free remission, five died—two from disease relapse and three from infection-associated hemophagocytic syndrome (Ann. Rheum. Dis. 2004;63:1318-26). ■

A Second Course of Rituximab Increases Clinical Efficacy in Rheumatoid Arthritis

AMSTERDAM — The clinical response to repeat courses of rituximab equalled or surpassed the initial course in patients with rheumatoid arthritis who are participating in a long-term open-label study, Dr. Paul Emery said at the annual European Congress of Rheumatology.

Patients with rheumatoid arthritis (RA) unresponsive to traditional disease-modifying antirheumatic drugs but who achieved at least a 20% improvement in tender and swollen joint counts following a single course of rituximab were eligible to receive additional courses for residual disease.

To date, 145 patients have received at least two courses, and 24-week follow-up data are available for 99. Each treatment course consists of two separate infusions, 1,000 mg each, 2 weeks apart.

Baseline characteristics of the 99 patients were similar to those of the original larger study population, where the mean age was 54 years and disease duration was 10 years.

Mean tender and swollen joint counts at baseline were approximately 32 and 20, respectively, and mean disease activity score including a 28-joint count (DAS28) was 6.8 (N. Engl. J. Med. 2004; 350:2572-81).

A total of 58 (59%) of patients had achieved an ACR20 response 24 weeks after the first course of rituximab, while 72 (73%) reached this level of response 24 weeks after the second course, according to Dr. Emery, professor of rheumatology and clinical director of the Academic Unit of Musculoskeletal Disease at the Leeds (England) Teaching Hospitals Trust.

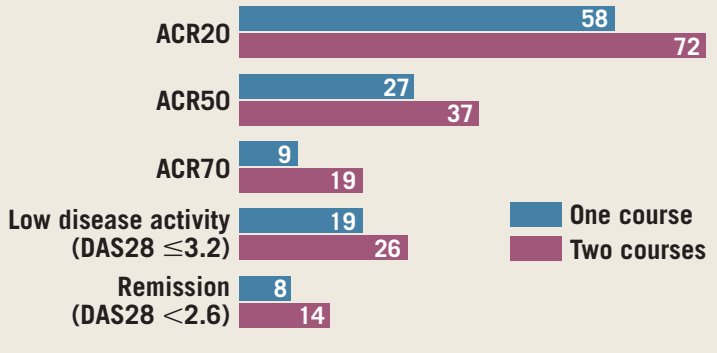
Maximal efficacy with rituximab generally is seen at 24 weeks.

Increased efficacy also was apparent on other measures. (See table.)

Repeat courses of the B-cell–depleting agent were well tolerated, and there was no evidence of increased overall incidence of adverse events, numbers of infections, or infusion reactions, he said.

—Nancy Walsh

Patients' Responses After One and Two Courses Of Rituximab Compared With Baseline



Note: Based on a study of 99 patients, after 24 weeks of treatment.
Source: Dr. Emery

ELSEVIER GLOBAL MEDICAL NEWS

Rituximab Changed Course Of Long-Standing Arthritis

AMSTERDAM — For the first time, rituximab has been shown to prevent the progression of joint damage—a critical therapeutic outcome—in patients with long-standing, intractable rheumatoid arthritis, Dr. Edward Keystone said at the annual European Congress of Rheumatology.

"This is the first time we've seen an agent that can inhibit radiographic progression after the failure of tumor necrosis factor blockade," said Dr. Keystone. Some 25%-40% of patients do not respond to tumor necrosis factor–α inhibitors.

In a double-blind trial that included 517 patients whose mean disease duration was 12 years, the mean change in total Sharp score from baseline was 2.31 among patients randomized to placebo plus methotrexate (10-25 mg/week) after 1 year of follow-up.

In contrast, among those receiving two infusions of rituximab, 1 g 2 weeks apart, plus background methotrexate, the mean change in Sharp score was 1, said Dr. Keystone, a professor of medicine at the University of Toronto. Mean changes in erosion scores were 1.32 and 0.59 in the placebo and rituximab groups, respectively, while mean changes in joint space narrowing were 0.99 and 0.41.

These differences were statistically significant and represented a 50% reduction in radiographic progression, he said at the meeting, sponsored by the European League Against Rheumatism.

Of the patients receiving rituximab, 61% had no change in erosion score from baseline, as did 52% of those receiving only methotrexate.

Clinical efficacy also was maintained among patients receiving rituximab, with 51%, 27%, and 12% of patients achieving ACR 20, 50, and 70 responses, respectively, according to Dr. Keystone.

The average time to flare was 30 weeks.

Rituximab is a selective inhibitor of CD20+ B cells. Its administration results in depletion of this subset of B cells, possibly through cell-mediated and complement-dependent mechanisms.

—Nancy Walsh