Careful Dosing May Boost Response to Infliximab

BY CHRISTINE KILGORE
Contributing Writer

Rheumatoid arthritis patients' response to treatment with infliximab may be improved by adjusting the dosage according to serum trough levels of infliximab, as well as to pretreatment levels of C-reactive protein, a study has indicated.

An open, prospective observational study of 105 consecutive patients with rheumatoid arthritis "confirms the relationship" between trough serum concentrations of infliximab and the extent of clinical improvement in patients taking the drug, reported G.J. Wolbink, M.D., of the Jan van Breemen Institute in Amsterdam, and associates.

The study also showed that levels of pretreatment C-reactive protein (CRP) correlate negatively with serum trough levels of infliximab and clinical response, they said.

"As infliximab is expensive, it might be efficient to adjust the infliximab dosing schedule after measurement of the serum infliximab concentration," the investigators said.

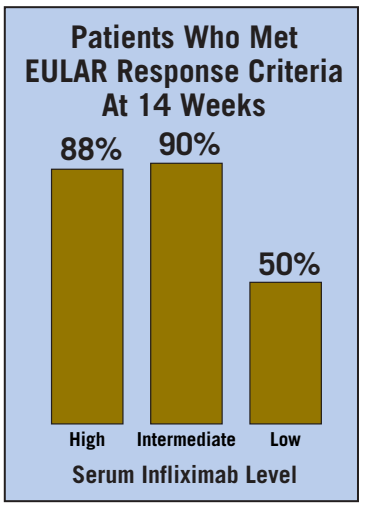
In addition, "patients with high pretreatment CRP levels might benefit from higher dosages of infliximab than patients with low CRP levels," they said (Ann. Rheum. Dis. 2005;64:704-7).

The investigators measured serum trough infliximab levels before intravenous infusions of 3 mg/kg infliximab, a TNF blocking treatment, at 0, 2, 6, and 14 weeks.

They assessed disease activity before each infusion using the 28-joint count Disease Activity Score (DAS28). In addition, they used European League Against Rheumatism response criteria to classify patients at 14 weeks as "responders" or "nonresponders," and they categorized patients into three groups according to their infliximab levels.

(Nonresponse was defined as a DAS28 decrease after 14 weeks of 0.6 or less, or a decrease between 0.6 and 1.2 with an attained DAS of greater than 5.1).

At 14 weeks, nonresponders had significantly lower median serum trough infliximab concentrations than responders (0.5 vs. 3.6 mg/L). The association remained significant after correction for potential confounders such as baseline CPR, baseline DAS28 score, and rheumatoid factor.



Moreover, patients categorized as having low infliximab levels at 14 weeks less often fulfilled the EULAR response criteria than patients with intermediate and high infliximab levels (50% vs. 90% and 88%). They also had significantly less improvement in the DAS28 score (–0.9 vs. –2.0 and –2.4).

Pretreatment levels of CRP—used as an indirect marker for TNF production—correlated negatively with infliximab levels at each dosage interval.

And during the last treatment interval (6-14 weeks) the change in the DAS28 score of patients with low pretreatment CRP levels differed significantly from that of patients with high pretreatment CRP levels (–0.2 vs. 0.6), the investigators reported.

The majority of patients were women (82%) with a mean disease duration of 12 years and a mean DAS28 score at entry of 6.1. Most had used methotrexate, and this as well as other stable drug treatments were continued during the study. ■

Adalimumab Shows Promise for Refractory Psoriatic Arthritis

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

New Orleans — Adalimumab appears to be an extremely effective treatment for both psoriasis and psoriatic arthritis, producing improvements of up to 80% in body surface area affected, Jennifer Cather, M.D., reported in a poster at the annual meeting of the American Academy of Dermatology.

"It is by far one of the best drugs we have tried for our refractory psoriasis patients," Dr. Cather said in an interview. "We are still waiting for the long-term safety data, though, so we have only used it on patients who didn't respond to other therapies."

Adalimumab is approved for refractory rheumatoid arthritis and marketed as Humira by Abbott Laboratories. Early trials of the usefulness of the tumor necrosis factor–α blocking agent in psoriasis were promising; several phase III studies are now underway. Dr. Cather of Baylor College of Medicine, Houston, participated in some of these trials, but presented data on her clinic's current experience with adalimumab in 24 psoriasis patients. "None of the people in this study were part of any clinical trials, because we did not want to bias the results by only including responders," she said.

All patients had either psoriasis or psoriatic arthritis, and all had failed at least one therapy, including cyclosporine, PUVA, methotrexate, alefacept, acitretin, hydroxyurea, sulfasalazine, isotretinoin, narrowband UVB, etanercept, prednisone, bexarotene, and infliximab.

At baseline, every patient underwent testing for HIV virus and hepatitis B and C, and every patient got a tuberculin skin test. Other baseline studies included electrolytes, liver function, and complete blood count.

Twelve patients are on adalimumab monotherapy. Their average age is 44 years, and average body surface area (BSA) at baseline was 25%. Six began monotherapy with 40 mg/wk; one patient decreased dosing to 40 mg every 3 weeks as maintenance therapy. Six patients started with 40 mg every other week; two of them escalated to weekly dosing for optimal disease control and one went to 40 mg every 3 weeks as maintenance therapy.

This group has received adalimumab for an average of 30 weeks (9-48 weeks). Their current average BSA is 7%, a 72% reduction from baseline.

Twelve patients are on adalimumab combination therapy. Their average age is 50 years and average BSA at baseline was 22%.

Concomitant therapies include cyclosporine (6), methotrexate (4), narrowband UVB (10), methotrexate and cyclosporine (1), and acitretin and cyclosporine (1).

Nine patients began combination therapy with 40 mg/week adalimumab. One patient decreased dosing to every other week, and two patients failed to taper to every other week.

The two patients on triple combination therapy successfully transitioned to adalimumab as monotherapy for maintenance. One patient transitioned off cyclosporine to adalimumab as maintenance monotherapy. Three other patients started combination therapy with 40 mg adalimumab every other week; two escalated to weekly dosing for optimal disease control. One patient decreased dosing to every 3 weeks as maintenance therapy.

Combination therapy patients have received adalimumab for an average of 24 weeks (6-81 weeks). Their current average BSA is 3.6%—an 80% reduction from baseline.

Adalimumab appears most effective in patients who have not previously been heavily treated, especially with biologics, Dr. Cather noted.

All tumor necrosis factor–α antagonists are associated with an increased risk of lymphoma. However, Dr. Cather stressed, studies showing that association include a very high proportion of rheumatoid arthritis patients, among whom lymphoma occurs at a rate of up to 24 times that of the background population. Psoriasis patients also have an increased risk of lymphoma, but at a much lower rate—only 2-3 times that of the background population. ■

Multiple Joint Involvement Shown As the Rule, Not the Exception

BY BRUCE JANCIN
Denver Bureau

Vienna — Multiple joint problems are the rule, not the exception, in individuals with joint pathology, Anne-Maree Keenan reported at the annual European congress of rheumatology.

She presented the results of a very large British primary care practice survey showing that the prevalence of one or more chronic joint problems was high in individuals older than 55 years—and that the median number of such problems in affected individuals was four.

Moreover, the degree of associated functional impairment in activities of daily living rose exponentially rather than additively as the number of joint problems increased, said Ms. Keenan, a podiatrist and research fellow in the academic unit of musculoskeletal disease and rehabilitation, University of Leeds, England.

These findings highlight the drawbacks of the typical assessment and treatment algorithms for joint pathology. Busy physicians often focus on a single major joint, thereby ignoring the true extent of the patient's problems.

"What we've found in interviewing people is that because they have such a short time in the physician's office, their knee problem is all they'll talk about, when in fact they have problems with other joints that go unaddressed," she told this newspaper at the meeting, which was sponsored by the European League Against Rheumatism.

Ms. Keenan reported on 16,222 community-dwelling British adults older than 55 years who completed a postal questionnaire about joint problems.

The research, funded by the U.K. Arthritis Research Campaign, was conducted under the auspices of the Leeds West Primary Care Trust. The survey response rate was 86%.

Participants were asked to report joint problems involving pain, swelling, and/or stiffness that lasted more than 6 weeks during the prior 3 months, and to rate the effect on activities of daily living.

The knee was the joint most frequently involved, with a prevalence of 220 per 1,000 population. However, the knee was the sole joint involved in only 1 of 11 affected individuals.

Far more commonly, knee pathology was reported in combination with problems in the hands, feet, back, and other joints.

Individuals with single joint pathology restricted to the knee were 3.7-fold more likely than respondents without joint problems to report significant difficulty in standing and walking.

But individuals with multiple joint problems involving the knees and feet were 14.5-fold more likely to have difficulty in standing and walking. And in those with problems affecting the knee, back, feet, and hips—a condition with roughly the same prevalence as isolated knee pathology in the survey population—the odds of difficulty in standing and walking shot up to 39-fold greater than in individuals without joint problems. ■