TNF-α Blockers May Cause Severe Skin Reactions

BY ALICIA AULT
Contributing Writer

Skin reactions to tumor necrosis factor-α–blocking drugs for rheumatoid arthritis might be more common and more varied than previous studies have indicated, results of a new prospective study show.

The study authors, from Radboud University Nijmegen (the Netherlands) Medical Centre, said theirs is the first large prospective study of skin conditions in rheumatoid arthritis (RA) patients taking TNF-α–blocking medications.

Overall, 25% of the 289 patients taking the biologics got a rash or infection, compared with 13% of the same number of control patients. The odds ratio for a patient taking the biologics to require a skin-care consultation was 2.26 (Arthritis Res. Ther. 2005;7:R666-76). The study was published online at BioMed Central's Web site on April 4.

There seemed to be no characteristic at baseline that predicted which patients might be susceptible to such rashes or infections, the authors said.

In the trial, 289 consecutive patients with RA who were started on TNF-α–blocking therapy—infliximab, etanercept, adalimumab, or the experimental agent lenercept—were compared with 289 patients from a cohort of 500 who have been followed at the medical center since 1985 but who had never taken a TNF-α–blocking agent.

Any patient who visited a dermatologist during the follow-up period was identified, and any new manifestation or exacerbation of a skin disease or any drug-related eruptions were recorded. The researchers also recorded diagnoses, topical and systemic therapeutic actions, outcome of the event, and any information on rechallenge.

Median follow-up time was 2.3 years. Among the patients taking anti-TNF therapy, 70 (24%) had received more than one agent, 8 (3%) had a history of taking more than two. Overall, 167 patients were given infliximab, 108 received adalimumab, 78 received etanercept, and 31 were treated with lenercept.

In total, there were 128 dermatologic events in the TNF group; 56 events occurred with adalimumab, 49 with infliximab, 16 with etanercept, and 13 with lenercept. Skin infections accounted for the largest proportion of these therapy-related events, with 33 fungal, bacterial, and viral infections recorded. TNF-α–blocking therapies are known to increase susceptibility to infections, and the study findings suggest that the immunosuppressive agents might also make patients more vulnerable to skin infections, said the authors.

Eczema was diagnosed 20 times in 19 patients, and 3 patients stopped therapy. One patient was hospitalized. The others were treated with topical corticosteroids.

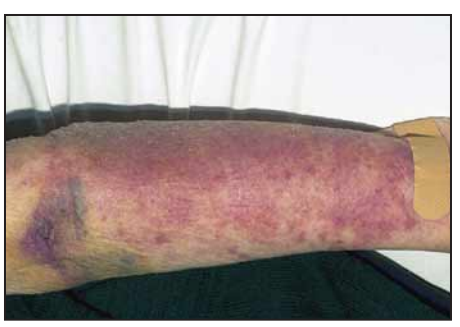
There were frequent cases of drug-related eruptions in the first 5 months, in particular, said the authors. Most common was a combination of exanthema, urticarial eruptions, lichenoid skin lesions, and purpura. Of 15 patients diagnosed with an eruption, 7 stopped therapy, and 8 continued. One was hospitalized.

In smaller numbers, patients also experienced ulcers, benign and malignant skin tumors, vasculitis, actinic keratosis, edema, chronic venous insufficiency/varices, xerosis cutis, and stasis dermatitis.

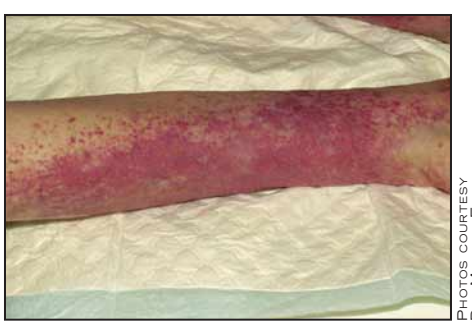
The occurrence of psoriasiform eruptions in three patients was "particularly interesting," given that etanercept is approved for psoriasis, and infliximab may soon get that approval, the researchers said.

The time between the start of therapy and onset of skin conditions varied, but some events looked more likely to be drug related, including the eruptions, cutaneous vasculitis, a case of systemic lupus erythematosus, dermatomyositis, and a lymphomatoid papulosis-like eruption.

Overall, 19 of the 72 patients who had skin problems stopped taking the TNF-α–blocking therapy, they said. ■



An eczematous reaction on the left arm of a patient on infliximab is shown.



A drug-related eczematous eruption is shown on a patient's leg after infliximab.

PHOTOS COURTESY DR. MARCEL FLENDRIE

Adalimumab Looks Good for Psoriasis

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 (Humira) is approved for refractory rheumatoid arthritis. Early trials of the drug's usefulness 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 didn't want to bias the results by only including responders," she said.

All of the patients had either psoriasis or psoriatic arthritis, and all had failed at least one previous form of 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. ■

Etanercept Improves Quality Of Life in Psoriatic Arthritis

NEW ORLEANS — Psoriatic arthritis patients receiving etanercept reported sustained clinical benefits for up to 2 years, according to data from an open-label extension study.

Patients treated with the drug reported inhibition of disease as well as significant improvements in physical functioning and quality of life, Philip J. Mease, M.D., reported at the annual meeting of the American Academy of Dermatology.

After an initial 24-week blinded phase of the study, 169 patients received 25 mg of etanercept (Enbrel) twice weekly for an additional 48 weeks during the open-label extension phase.

Patient-reported outcomes included the physical and mental components of the Short-Form (SF-36) Health Survey and the Health Assessment Questionnaire–Disability Index (HAQ-DI). During the placebo-controlled phase, etanercept-treated patients had a mean improvement of 9.3 points on the SF-36 physical component summary scale, whereas placebo patients improved only 0.7 on the scale.

In the open-label phase, patients originally randomized to etanercept maintained their improvements (mean 12.6 points), and patients switched to etanercept from placebo improved almost to the same level as those on continuous etanercept, said Dr. Mease, a rheumatologist at the Swedish Medical Center, the University of Washington, Seattle. Both groups had normal mental health at baseline and maintained it throughout the industry-sponsored trial.

In the placebo-controlled phase, the HAQ-DI improved from 1.1 to 0.5 in the etanercept group and from 1.1 to 1 in the placebo group. At 48 weeks, 40 (53%) of 75 patients originally randomized to etanercept had an HAQ-DI of zero, indicating no disability in performing activities of daily living. The mean HAQ-DI score at 48 weeks was 0.4 for patients continuously treated with etanercept and 0.6 for 70 patients switched from placebo to the drug.

Eleven patients originally randomized to placebo and 10 patients on continuous etanercept dropped out of the open-label phase.

A change of 0.3 in the HAQ score is considered a minimal clinically important difference. Thus a change of 0.6 in the etanercept group "clearly was highly clinically meaningful to the patients," said Dr. Mease, who receives grant support and is a consultant and member of the speaker's bureau for Amgen, which manufactures Enbrel.

—Patrice Wendling