Alefacept Boosts Response To Methotrexate in Patients With Psoriatic Arthritis

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CHICAGO — The combination of methotrexate and alefacept appears to be safe and effective for the treatment of psoriatic arthritis, Mark G. Lebwohl, M.D., said at the 11th International Psoriasis Symposium, sponsored by the Skin Disease Education Foundation.

This is the first study to evaluate alefacept in combination with methotrexate in psoriatic arthritis, which affects about 20%-30% of all psoriasis patients.

At week 24, 54% of combination therapy patients achieved ACR 20, compared with 23% of the participants who received methotrexate plus placebo.

Alefacept (Amevive) is approved for psoriasis and demonstrated clinical improvement in an initial pilot in psoriatic arthritis.

In this double-blind study, 185 patients aged 18-70 years with active psoriatic arthritis despite methotrexate treatment for 3 or more months were randomized to 15-mg alefacept once weekly for 12 weeks or placebo. All patients continued on methotrexate at various dosages.

At week 14, 53% of patients in the alefacept group achieved a 50% or greater improvement according to scores on the Psoriasis Area and Severity Index (PASI 50), compared with 17% of the placebo group.

At week 24, 54% of the alefacept/methotrexate–treated patients achieved at least a 20% improvement according to American College of Rheumatology response criteria (ACR 20), compared with 23% of the investigation participants who received methotrexate plus placebo.

Results on both efficacy end points were statistically significant, he said.

The incidence of serious adverse events was 2%, and no serious infections or malignancies were reported in the alefacept-treated group.

Longer-term data for psoriasis shows no increase in malignancies or infections, Dr. Lebwohl noted in an interview. This suggests that the combination of alefacept and methotrexate may be useful in the long-term management of psoriatic arthritis.

In addition to greater efficacy, it's hoped that the combination therapy would allow for reduced methotrexate dosages, he said.

Two other biologic therapies, etanercept and infliximab, have both been used with methotrexate in rheumatoid arthritis, allowing for a reduction in the required dosage of methotrexate.

The rationale for using alefacept is that it selectively reduces memory T-cells, which may play a role in the pathogenesis of psoriatic arthritis, said Dr. Lebwohl, chair of dermatology at Mt. Sinai School of Medicine, New York.

Synovial fluid analyses from psoriatic arthritis patients have shown a reduction in CD4+ and CD8+ cells from baseline following treatment with alefacept. Other T-cell therapies, such as cyclosporine, also have shown some benefit in psoriatic arthritis patients.

Although it's not surprising that therapies targeting T cells might be of benefit in psoriatic arthritis, Dr. Lebwohl noted that a recent efalizumab (Raptiva) trial involving psoriatic arthritis patients did not show similar significant benefits.

Dr. Lebwohl is a consultant, speaker, and investigator for Biogen Inc., which markets alefacept. The SDEF and this newspaper are wholly owned subsidiaries of Elsevier. ■

Strategy Reduces Need for Monitoring Alefacept Users

CHICAGO — Assessing CD4 T cells at week 4 during the treatment of psoriasis with alefacept can reduce the need for further lymphocyte monitoring in some patients, Jennifer Cather, M.D., reported at the International Psoriasis Symposium sponsored by the Skin Disease Education Foundation.

The strategy could also lower costs and make alefacept therapy more convenient, she added.

Weekly CD4 counts are required by the alefacept (Amevive) package insert throughout the 12-week treatment regimen and are done as standard of care.

Dr. Cather suggested that the counts at week 4 can predict with a high degree of accuracy what the counts for weeks 5-12 will be.

If the count is more than 600 cells/μL at week 4, there is less than a 0.1% chance of having a subsequent CD4 count fall below 250 cells/μL, Dr. Cather said.

Therefore, she explained, weekly monitoring during the remaining treatment may be unnecessary in these patients.

Monitoring should be performed monthly for patients with a count between 400 cells/μL and 600 cells/μL, and every 2 weeks if the count is less than 400 cells/μL at week 4.

If a patient's CD4 count is less than 250 cells/μL at any time during alefacept treatment, the drug is usually withheld and testing should be done weekly until the count is 250 cells/μL or greater.

The recommendations are from a proposed monitoring algorithm based on a mathematical model and later confirmed at Baylor University Medical Center at Dallas, where Dr. Cather is codirector of the cutaneous lymphoma and graft vs. host disease clinic.

Biogen Idec, which makes alefacept, revised its package insert for the biologic last year after concerns were raised about serious liver injury in two patients. It is important to monitor for liver enzyme elevations in patients with psoriasis and psoriatic arthritis, said Dr. Cather, who has received funding support from Biogen Idec.

"I think that the hepatotoxicity that we see with a lot of these biologics is because the patient's liver is different," she said. "Perhaps the increased hepatotoxicity is a result of increased body mass index and steatohepatitis."

Ongoing trials are evaluating whether longer treatment with alefacept is needed to improve its efficacy, suggesting that long-term monitoring will remain important for physicians and patients.

Early data suggest that the addition of four doses to the 12-week treatment regimen increased response rates in patients with psoriasis, and that multiple courses may improve clinical responses in psoriasis patients who fail to show a strong initial response, she said.

"In addition, there are some data that show that their duration of remission in between each course improves with multiple courses," said Dr. Cather.

In 197 patients with psoriasis who received 264 courses of alefacept at Baylor University independent of clinical trials, CD4 counts did not fall below 400 cells/μL in any of the patients, she said.

A total of 109 (41%) of treatments were 12-week courses of alefacept in combination with other therapies, including methotrexate, cyclosporine, hydroxyurea, ultraviolet B light, and acitretin. A total of 83 (32%) were standard 12-week alefacept monotherapy courses; 63 (24%) were extended courses of alefacept for 12 or more weeks either as monotherapy or in combination with other agents; and 8 (3%) were double-dose or alternative-dosing regimens.

The most common adverse events were fatigue, joint pain, aches, and chills.

There were five cases of infection, four malignancies including three skin cancers and one case of lung cancer, and no cases of liver or kidney toxicity.

Dr. Cather noted that in a recent case report of alefacept in two patients with hepatitis C infection and psoriasis, decreases in CD4 and CD8 counts were transient, and were not associated with either an increase in hepatitis viral loads or exacerbation of infection (Br. J. Dermatol. 2005;152:1048-50).

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Etanercept Found Safe in Patients With Concurrent Hepatitis C

NEW ORLEANS — Etanercept appears to be a safe therapeutic option in psoriasis patients with concurrent hepatitis C, according to the results of a retrospective case series.

"Not only does it appear to be safe, it might even be beneficial for the patient's underlying hepatitis," Erin J. Allen, M.D., proposed during a poster presentation at the annual meeting of the American Academy of Dermatology.

Hepatitis viral loads decreased in two of the five patients receiving etanercept (Enbrel) 25 mg twice weekly for up to 14 months. Three patients had decreased liver transaminases.

Of the two patients with elevated transaminases, one discontinued interferon prematurely just before starting etanercept, so the worsening transaminases were not unexpected, said Dr. Allen, a dermatologist at St. Louis University. In the other patient, a significant elevation was noted only in alanine transaminase and not in the transaminase levels.

All patients showed marked improvement of their psoriasis, with three of the five patients becoming "clear" or "almost clear" on the physicians' global assessment.

Two patients experienced a flare when started on interferon, but still tolerated the interferon, and psoriasis remained less than 10% of body surface area.

Etanercept, an anti–tumor necrosis factor (TNF) therapy, was a rational choice for these patients because TNF is elevated in both hepatitis C and psoriasis, said Dr. Allen, who has participated in etanercept trials, but didn't receive funding for the series.

Although the exact mechanism is not known, etanercept neutralizes the proinflammatory effects of TNF by preventing soluble TNF-α and TNF-β from binding to their receptors.

The case series joins a very limited amount of literature evaluating the use of etanercept (Enbrel) in patients with rheumatoid arthritis (RA) or psoriasis and concurrent hepatitis C (HCV).

According to the literature, treatment with etanercept did not worsen the underlying hepatitis in three psoriasis patients (J. Am. Acad. Dermatol. 2004;51:580-4) and improved the serum transaminases and viral loads in some patients with RA and HCV (J. Dermatolog. Treat. 2003;14:229-32).

Although etanercept was generally well tolerated, Dr. Allen recommended that all psoriasis patients with concurrent hepatitis C be closely monitored in conjunction with a hepatologist until more data are available. ■