Extended Efalizumab for Psoriasis Well Tolerated

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Efalizumab appears to be well tolerated over the course of up to 60 weeks of treatment, according to a combined analysis of more than 1,000 patients with moderate to severe chronic plaque psoriasis.

Common adverse events were similar to those seen in shorter trials; no new category of common adverse event appeared during extended therapy periods, Dr. Alice B. Gottlieb reported in a poster session at the annual meeting of the American Academy of Dermatology.

The risk of serious adverse events did not increase over time, added Dr. Gottlieb of the University of Medicine and Dentistry of New Jersey, New Brunswick, N.J. Dr. Gottlieb is a paid consultant for Genentech Inc., which makes efalizumab (Raptiva). The Food and Drug Administration approved the biologic agent for the treatment of moderate to severe psoriasis in October 2003.

The analysis appears to be the largest compilation of psoriasis patients studied through 60 weeks of treatment with a biologic therapy.

Dr. Gottlieb and her associates evaluated the long-term safety of efalizumab, injected subcutaneously at weekly intervals, by pooling the 60-week data from two multicenter phase III studies of adults with moderate to severe chronic plaque psoriasis. The Psoriasis Area and Severity Index (PASI) of the patients was at least 12 at baseline; their mean PASI was 19. At least 10% of their body surface area was affected; the mean was 29%.

One study was a 60-week randomized, double-blind, parallel-group, placebo-controlled trial. Included in the pooled analysis were 450 patients who had been randomized to receive efalizumab during the 12-week placebo-controlled portion of the trial and 218 who were randomized to receive placebo. Both groups entered an open-label extended-treatment phase for up to 48 weeks of active treatment, and then were eligible to continue to receive the drug for another 12 weeks or until the drug became commercially available.

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DR. GOTTLIEB

The second study included in the pooled analysis was an open-label 36-month trial. The investigators evaluated safety data for up to 60 weeks of therapy for 339 of the patients.

Concomitant use of topical psoriasis therapy or phototherapy was permitted at various periods in both studies. For analysis, the investigators divided treatment phases into five consecutive 12-week segments. During the first 12-week exposure period, 80% of 1,004 patients experienced at least one adverse event. These occurred most often within 48 hours of efalizumab injection, and consisted primarily of headache, fever, chills, nausea, pharyngitis, and a flulike syndrome. The percentage of patients experiencing an adverse event then gradually decreased to 48% among the 537 patients followed for 49-60 weeks, Dr. Gottlieb wrote.

Infections occurred in 20%-30% of patients during each of the five evaluation periods. Arthritis occurred in 1%-3% of patients throughout the five periods.

Serious adverse events were noted in 2%-3% of patients during each 12-week segment. The incidence of each serious event was less than 1%, except for serious skin-related problems, which peaked at 1% during the 37-48 week exposure period. There was one case of hemolytic anemia that occurred with 25-36 weeks of exposure. Eight cases of thrombocytopenia were reported; two occurred during the first 12 weeks of exposure, three with 13-24 weeks, two with 25-36 weeks, and one with 37-48 weeks of exposure.

The incidence of malignancy remained at less than 1% throughout. The most common malignancy was nonmelanoma skin cancer, of which there were 18 cases, Dr. Gottlieb reported. ■

New Psoriasis Drugs May Boost Compliance

BY BRUCE JANCIN
Denver Bureau

KOLOA, HAWAII — With the plethora of topical clobetasol propionate formulations already on the market, why do physicians and patients need the recently approved Clobex spray that's now reaching pharmacy shelves?

"Compliance, compliance, compliance," Dr. Chai Sue Lee said at the annual Hawaii Dermatology Seminar sponsored by the Skin Disease Education Foundation.

A 2005 survey from the National Psoriasis Foundation showed that 73% of psoriasis patients, regardless of disease severity, are less than "very satisfied" with their current treatment.

Clobetasol propionate is already the most commonly prescribed topical corticosteroid for moderate to severe psoriasis in the United States and Europe. Some patients will find the new clobetasol propionate 0.05% spray (Clobex spray) more user friendly than other formulations of the drug. And increased patient satisfaction is likely to translate into improved treatment compliance, explained Dr. Lee, director of the psoriasis treatment center at the University of California, Davis.

In two multicenter phase III randomized, double-blind, vehicle-controlled, and Galderma-sponsored clinical trials, twice-daily Clobex spray resulted in a high rate of durable treatment responses. Indeed, 72% of Clobex spray responders in one study and 76% in the other remained clear, almost clear, or with only mild psoriasis, a full 4 weeks after the end of 4 weeks of therapy. Adverse events were similar in the Clobex and control groups.

The prospect of better compliance is also a major selling point for the combination calcipotriene/betamethasone dipropionate approved by the FDA earlier this year. The two drugs aren't ordinarily compatible due to differing pH requirements. However, Warner-Chilcott came up with a water-free vehicle that allows for a stable combined product.

In the United States, the combination is known as Taclonex. In Europe and Canada, where it has been available as Dovobet or Daivobet for several years, it has rapidly grabbed market share. The widespread use is attributed in part to the fact that the combination product is highly effective as once-daily therapy, which confers a significant compliance advantage over other psoriasis topicals. Moreover, once-daily dosing means half the exposure to drug side effects, compared with twice-daily dosing, as well as lower medication volume and cost, Dr. Lee continued.

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Taclonex is one of the most extensively studied topical agents in the world. It has been the subject of seven completed international clinical trials totaling more than 7,000 psoriasis patients. A recent metaanalysis involving six of these double-blind randomized trials totaling more than 6,000 psoriasis patients concluded that 4 weeks of therapy with the two-compound product resulted in 65%-74% reductions in the Psoriasis Area and Severity Index, significantly better than with either agent alone. The tolerability profile was similar to betamethasone monotherapy and better than with calcipotriol alone (J. Eur. Acad. Dermatol. Venereol. 2006; 20:39-44).

The studies demonstrated Taclonex was effective not only for acute flares, but also as maintenance therapy in a 52-week trial.

"Also, for those of us who do not feel comfortable prescribing a class-2 steroid like betamethasone for long-term maintenance, another strategy would be to switch to intermittent therapy with weekday calcipotriol and weekend Taclonex, or even just calcipotriol monotherapy once the disease has been gotten under control," Dr. Lee said.

Yet another intriguing development in topical therapy is an over-the-counter (OTC) hydrogel patch modified by the addition of an impermeable coating on one side. The goal is an inexpensive, user-friendly form of occlusive therapy for psoriasis.

Preliminary results of a 120-patient, open-label right/left comparison study by University of California, San Francisco, dermatologists showed that the patch readily covered hard-to-wrap areas such as the elbow. The patch alone resulted in substantial improvement in mild psoriasis lesions. Moreover, when the patch was applied over OTC 1% hydrocortisone, tacrolimus 1% ointment, or more potent topical agents, the result was in every case superior to the drugs alone, according to Dr. Lee.

Dr. Lee disclosed that she has conducted research sponsored by Warner-Chilcott.

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Adalimumab Helps Skin Disease in Psoriatic Arthritis

SAN FRANCISCO — Adalimumab is effective in treating both mild to moderate and moderate to severe skin disease in patients with psoriatic arthritis, Dr. Dafna D. Gladman reported in a poster presentation at the annual meeting of the American Academy of Dermatology.

Adalimumab, a tumor necrosis factor blocker, was approved in 2005 for the treatment of rheumatoid arthritis and psoriatic arthritis. To assess whether the level of skin disease affected the response of psoriasis to the drug, Dr. Gladman and her associates performed a post-hoc analysis of a 24-week, placebo-controlled phase III trial of patients with moderately active to severely active psoriatic arthritis.

Among those in the adalimumab-treated group, 53 patients had mild to moderate skin disease, with a Psoriasis Area and Severity Index (PASI) score of less than 10 at baseline; 16 patients had moderate to severe skin disease, with a PASI score of 10 or more.

PASI responses occurred quickly and were maintained. After 24 weeks of drug treatment, the two subgroups had similar response rates. Comparing the mild/moderate and moderate/severe groups, a PASI 50 score (a 50% reduction from baseline) was achieved by 39 (74%) and 13 (81%), respectively; a PASI 90 score was achieved by 23 (43%) and 6 (38%) in the respective groups, reported Dr. Gladman of the University of Toronto.

Dr. Gladman is a primary investigator for Abbott Laboratories, which makes adalimumab (Humira).

Both subgroups, she said, achieved "meaningful improvements" in quality of life, compared with baseline, as measured by the Dermatology Life Quality Index.

—Sherry Boschert