Topical May Boost Adalimumab Effect in Psoriasis

ARTICLES BY BRUCE JANCIN

BERLIN — Psoriasis patients randomized to adalimumab plus adjunctive topical therapy experienced significantly greater reduction in disease severity and greater quality-of-life improvements through the first 4 weeks of therapy than those on adalimumab plus vehicle in the BELIEVE trial.

Adding fixed-dose combination topical calcipotriol/betamethasone dipropionate ointment to adalimumab brought more rapid initial improvement, compared with adalimumab monotherapy, but the advantage was not sustained.

From week 8 through week 16, when the study concluded, most outcomes in the two treatment arms were no longer statistically different. And in the few end points where there was a significant difference at week 16, adalimumab monotherapy—not combination treatment—was the winner, Dr. Diamant Thaçi reported at the annual congress of the European Academy of Dermatology and Venereology.

BELIEVE was a phase IIIb randomized, double-blind clinical trial involving 730 European patients with moderate to severe psoriasis who had previously failed two or more classic nonbiologic systemic therapies. In addition, more than half of the subjects had a history of prior therapy with one or more anti–tumor necrosis factor (TNF) drugs, noted Dr. Thaçi of Johann Wolfgang Goethe University, Frankfurt.

All participants received an initial 80-mg subcutaneous dose of adalimumab (Humira), followed by a 40-mg dose every 2 weeks. In addition, they were randomized to topical calcipotriol/betamethasone (Taclonex, Dovobet, Daivobet) or placebo applied once daily during the first 4 weeks, then on an as-needed basis.

Clinical improvement came significantly more swiftly with the biologic/topical therapy combination.

DR. THAÇI

The primary study end point—a 75% improvement from baseline in Psoriasis Area and Severity Index (PASI-75) scores at week 16—was achieved by 64.8% of patients in the combination arm and a statistically similar 70.9% of those on adalimumab plus vehicle, Dr. Thaçi said.

This week-16 trend favoring monotherapy for PASI-75 achieved significance for PASI-90: a 50.3% rate with monotherapy, compared with 38.8% with combination therapy, he said. The week-16 PASI-100 rate of 24% with monotherapy also was significantly better than the 15% with combination therapy.

"I cannot explain the reason for this at the moment, but I hope in the near future we'll have more explanation about this after we finish ongoing subanalyses," Dr. Thaçi said.

Of importance to long-suffering patients, however, clinical improvement came significantly more swiftly with the biologic/topical therapy combination. The PASI-75 rate at week 2 was 14.8% with combination therapy and 5.8% with adalimumab monotherapy. At week 4, the PASI-75 rate was 40.7% with combination therapy, compared with 32.4% with monotherapy.

Similarly, initial improvements in various patient-reported quality-of-life measures were significantly greater through week 4 with combination therapy. The implication is that combined biologic/topical therapy for the first month is advantageous but after that it has no benefit, he said.

From a mean baseline score of 14 on the 30-point Dermatology Life Quality Index (DLQI), at week 2 the combination therapy group showed a 47.5% improvement, significantly better than the 32.1% with adalimumab plus placebo. At week 4, the between-group difference remained significant: a mean 60.9% improvement on DLQI over baseline with combination therapy, compared with 46.6% with monotherapy. At week 16, patients on combination therapy had a mean 67.2% improvement, similar to the 71.5% with monotherapy, said Dr. Thaçi.

At week 2, patients in the combined therapy arm had a mean 60% reduction from baseline on visual analog pruritus scores, markedly better than the 37.5% decrease with monotherapy. The advantage in favor of combination therapy was maintained at week 4, with a 75% reduction in pruritus, as compared with 57.1% for monotherapy. By week 16, however, the reductions of 83.3% with combination therapy and 88.9% with monotherapy were statistically similar.

The same pattern was seen with regard to change over time in visual analog pain scores, he said.

The week-16 PASI-75 rate was 71.7% in anti-TNF-naive patients and nearly as good in patients with prior anti-TNF therapy, with a 65% PASI-75 in previous etanercept (Enbrel) users and a 59% rate in those with a history of infliximab (Remicade) use, Dr. Thaçi noted.

BELIEVE was sponsored by Abbott (manufacturer of Humira), and the topical calcipotriol/betamethasone was provided by LEO Pharma. Dr. Thaci is a consultant to Abbott. ■

Psoriasis Comorbidities Carry Steep Price Tag

BERLIN — More than half of psoriasis patients in a large managed care database had at least one nondermatologic comorbidity, reported Dr. Alexa Boer Kimball.

The psoriasis patients with comorbid conditions imposed a significant economic burden above and beyond that of patients with psoriasis of comparable severity but no comorbidities, Dr. Kimball reported at the annual congress of the European Academy of Dermatology and Venereology.

During the 6-month study period psoriasis patients with comorbidities had an adjusted 2.3-fold greater hospitalization rate, made 1.6-fold greater use of the emergency department, and had 1.5-fold more outpatient visits.

Psoriasis patients with one or more comorbidities incurred an average $2,184 more in total health care costs during the study than patients free of comorbidities. But this figure varied widely depending on the specific comorbidity.

The disparity was greatest for psoriasis patients with comorbid cerebrovascular disease, whose total costs averaged $6,191 more than psoriasis patients with no comorbidities, according to Dr. Kimball of the department of dermatology at Harvard Medical School in Boston.

The study included 114,512 adult psoriasis patients in the Ingenix Impact National Managed Care Database for 1999-2004. A total of 50.9% of the study patients had one or more of the comorbid conditions that were of interest to the investigators.

The two most common comorbidities were hyperlipidemia and hypertension, each affecting about one-quarter of the psoriasis patients. Next was depression, with a 9.2% prevalence rating during the 6-month study period, followed by diabetes, at 8.7%. The diagnosis of psoriatic arthritis was present in the records of 5.1% of patients, she noted.

A diagnosis of cerebrovascular disease was carried by 3.1% of patients. Peripheral vascular disease and cardiovascular disease, the second and third most expensive comorbidities, with incremental costs of $5,381 and $5,280, respectively, were present in 2.8% and 8.6% of psoriasis patients. Individuals with comorbid cardiovascular disease had a hospitalization rate 4.2-fold greater than those without cardiovascular disease.

Interestingly, conventional wisdom holds that psoriasis patients are more overweight than the general population, but it was not confirmed in this study, as the prevalence of obesity was just 3.8%, said Dr. Kimball.

She is a consultant to Abbott, which funded the study. ■

Rupatadine, an Allergy Drug, Tames Acquired Cold Urticaria

BERLIN — A drug known to be beneficial in the treatment of allergies has also proved effective and well-tolerated for the treatment of acquired cold urticaria in a randomized, double-blind, placebo-controlled crossover study.

Rupatadine is a dual antagonist of histamine and platelet activating factor (PAF) that has shown promising results in a clinical trial.

"We hypothesize that anti-platelet activating factor activity may contribute to the excellent clinical effect we saw in this trial," Dr. Martin Metz said at the annual congress of the European Academy of Dermatology and Venereology.

Patients who have cold urticaria respond to exposure to cold temperatures with erythematous wheals, severe itching, and mucosal swelling. The symptoms typically last from 30 minutes to 3 hours. Each patient has an individual critical temperature threshold: that is, the highest temperature that elicits wheals.

Rupatadine (Rupafin) resets the critical temperature threshold markedly downward in patients with cold urticaria, which is a benefit of great practical significance, said Dr. Metz, of Charité University Hospital, Berlin. For Northern Europeans with the disorder, it can mean the difference between being able to take a summertime swim in the nearby Baltic Sea instead of having to go to the Mediterranean, he said.

He reported on 21 patients with acquired cold urticaria at two medical centers who were randomized to 20 mg of rupatadine daily or placebo for 1 week in the Acquired Cold Urticaria and Rupatadine Efficacy (ACURE) study. After a 2-week washout period, they were crossed over to the other study arm.

Treatment response was objectively measured using TempTest, a programmable device Dr. Metz described as "an electronic ice cube" placed against the skin. The mean critical temperature threshold of participants at baseline and on placebo was 15 degrees C, but while on rupatadine, it dropped to below 4 degrees C, the lowest temperature employed for safety reasons.

At baseline, 13 patients had moderate-to-severe pruritus. During the rupatadine phase of the study, three patients had moderate pruritis and none had severe. Patients on rupatadine also experienced a significant reduction of cutaneous burning sensation.

During the rupatadine phase of ACURE, four patients reported mild fatigue, one complained of somnolence, and one patient reported a headache.

ACURE was sponsored by Uriach Pharma.It is not currently available in the United States. Dr. Metz is a consultant to the company. ■