Ustekinumab Aids Long-Term Control of Psoriasis

BY SHARON WORCESTER
Southeast Bureau

SAN ANTONIO — Long-term, continuous use of ustekinumab for maintenance therapy in patients with moderate to severe plaque psoriasis is efficacious and generally well tolerated, according to phase III study findings reported at the annual meeting of the American Academy of Dermatology.

The results of the PHOENIX I trial, a randomized, double-blind, placebo-controlled crossover trial of the novel human monoclonal antibody against interleukins 12 and 23, showed treatment response was better maintained at 76 weeks in responders who received 45 mg or 90 mg of ustekinumab every 12 weeks, compared with those who stopped treatment at 40 weeks, Dr. Kenneth B. Gordon of Northwestern University, Chicago, said in a poster session.

The drug's maker (Centocor Inc.) announced last month that its Biologics License Application for ustekinumab (CNTO 1275) had been accepted for review by the Food and Drug Administration.

The results of another phase III study of the drug (PHOENIX II), reported in October at the World Congress of Dermatology in Buenos Aires, showed ustekinumab was effective and safe in more than two-thirds of 1,230 patients with moderate to severe disease who received two subcutaneous doses of the drug. A 75% improvement in the psoriasis severity area index score (PASI 75) was achieved in 67% of patients randomized to receive 45-mg doses, 76% of those randomized to receive 90-mg doses, and 4% of those in the placebo group.

For the current study, 766 patients were randomized to receive placebo or 45 mg or 90 mg of subcutaneous ustekinumab at weeks 0 and 4 of the study, and then every 12 weeks thereafter. At the 12-week mark, those in the placebo group crossed over to receive 45 mg or 90 mg of ustekinumab then and at week 16 and then every 12 weeks thereafter.

At 40 weeks, the 160 patients in the 45-mg treatment group from baseline and the 161 in the 90-mg treatment group from baseline who achieved a PASI 75 response at weeks 28 and 40 were further randomized to ongoing treatment or placebo every 12 weeks.

Of those in the ongoing treatment groups, 96% maintained at least a PASI 50 score through week 76, compared with just over 30% in the placebo groups; PASI 75 and 90 scores were also maintained in more patients in the ongoing treatment groups, compared with the placebo groups (see chart). At 40 weeks, about 75% of the 90-mg group had disease rated as cleared or minimal on the Physician's Global Assessment.

Maintenance therapy with ustekinumab was well tolerated in this study at both the 45-mg and 90-mg doses, and safety was "generally comparable" with that with interrupted therapy after 40 weeks in both groups, noted Dr. Gordon, who received research support for the study from Centocor. No cases of tuberculosis, anaphylactic or serum sickness-like reactions, or injection-site reactions occurred. The most common adverse events were upper respiratory tract infection, nasopharyngitis, arthralgia, and headache (see chart).

Patients in PHOENIX I were at least 18 years old, had been diagnosed with plaque psoriasis for at least 6 months (most had a disease duration of about 20 years), had a baseline PASI score of 12 or higher, and had at least 10% body surface area involvement. Those with nonplaque forms of psoriasis, with a recent serious systemic or chronic infection, a history of tuberculosis, or a known malignancy were excluded. Baseline disease characteristics were similar across the groups, with 23%-25% body surface area involvement and baseline PASI scores of 19-20 in all groups.

Baseline Dermatology Life Quality Index (DLQI) scores were 11 or 12 in all groups and improved markedly when the PASI 75 primary end point was reached. But in those switched from treatment to placebo in the randomized withdrawal phase, DLQI scores returned to baseline even in those whose PASI scores were above baseline. "This means when people get better, they don't want to get worse again," Dr. Gordon said in an interview. "Even with clinical improvement … they are no longer tolerant of the amount of psoriasis they once had."

The findings show that the drug might "control plaque psoriasis with as few as four injections a year," he noted in a press statement. The drug targets different proteins involved in the inflammatory process and development of psoriasis. "The molecule attacks, binds to, and inactivates interleukin 12 and 23. The latter is important in activating the immune process and impacting the keratinocyte response, which are seen as the clinical manifestations of psoriasis. ■

Responses to Ustekinumab Maintenance Treatment

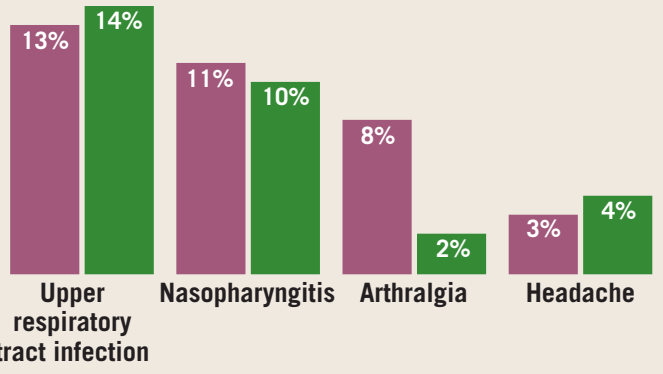
	Placebo (n = 73)	45 mg (n = 77)	Placebo (n = 87)	90 mg (n = 85)
PASI 75				
Week 52	64%	87%	62%	91%
Week 64	29%	80%	34%	90%
Week 76	20%	82%	18%	87%
PASI 50				
Week 52	86%	97%	83%	98%
Week 64	46%	93%	48%	96%
Week 76	31%	96%	32%	96%

Note: Psoriasis Severity Activity Index Scores are based on a study of patients with moderate to severe plaque psoriasis.

Source: Dr. Gordon

ELSEVIER GLOBAL MEDICAL NEWS

Common Adverse Events After 40 Weeks Of Treatment for Plaque Psoriasis



Source: Dr. Gordon

ELSEVIER GLOBAL MEDICAL NEWS

History, Physical Are Cornerstones of Melanoma Follow-Up

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — When it comes to follow-up surveillance of melanoma patients, history and physical examination remain the cornerstone of good care, with little solid evidence to support anything else.

"The literature on this aspect of melanoma management is incomplete, mainly because there are very few prospective studies," Dr. Peter R. Shumaker said at a melanoma update sponsored by the Scripps Clinic. He discussed several goals for postoperative follow-up:

▶ **Earliest possible detection of treatable recurrence.** About one-quarter of patients with local disease and 60%-70% of patients with in-transit [and] nodal disease will develop recurrence, said Dr. Shumaker, clinical fellow in procedural dermatology at the Scripps Clinic in La Jolla, Calif.

One study that reviewed the rate of first recurrence after treatment for malignant melanoma in 250 Australian patients found that 52% of recurrences were in the regional lymph nodes, 17% were local, 8% were in-transit, and 23% were visceral (Plast. Reconstr. Surg. 1993;91:94-8). Most recurrences occur within the first couple of years, he said, adding that patients are never considered unequivocally cured.

▶ **Detection of other primary skin cancers.** "These patients are at high risk for a second primary melanoma," Dr. Shumaker warned.

▶ **Patient education, emotional support, and reassurance.** Most data show that at least half of recurrences are found by the patients themselves, despite being in a structured follow-up program. "These follow-ups, [provide] an opportunity to inspect and palpate lesions [and] educate patients."

▶ **Quality assurance.** By this Dr. Shumaker meant the collection of data to improve future treatment and surveillance strategies, such as blood tests and imaging techniques. Chest x-rays and blood tests are often used in the routine follow-up of melanoma patients, "but offer little benefit in terms of cost effectiveness," he said. They generally provide low sensitivity and a high rate of false positives. "Even if occult metastases are found, there is no clear evidence that there is an overall survival benefit with these tests. Even if abnormal, blood tests are rarely the sole indicator of recurrent disease."

Most data show that at least half of recurrences are found by the patients themselves.

DR. SHUMAKER

Dr. Shumaker considers ^{18}fluorodeoxyglucose positron emission tomography (FDG-PET) combined with computed tomography a "promising" whole-body imaging technique for follow-up in high-risk patients or in symptomatic patients at any stage. The technique can detect subclinical metastases because of their elevated metabolic activity but has limited sensitivity in tumors 5 mm or smaller.

Ultrasound seems "more sensitive than physical exam in detecting tumor recurrence in in-transit routes and regional nodal basins. There is an increased likelihood of survival benefit from asymptomatic detection in these areas." He noted that ultrasound can be combined with fine-needle aspiration to diagnose recurrent or metastatic disease, but there appears to be no role for abdominal ultrasound in routine follow-up.

At Scripps, Dr. Shumaker and his associates perform a comprehensive history and physical exam in melanoma patients every 3 months for 3 years, then every 6 months for life. "This includes baseline and an annual chest x-ray and lab tests," he said.

They refer patients with high-risk, thick melanomas to their colleagues in hematology/oncology. "We have a very low threshold for obtaining additional studies in symptomatic patients. Many patients with high-risk melanoma have a baseline FDG-PET/CT scan. You could consider that for your high-risk patients in follow-up." ■