Omalizumab Quelled Urticaria in 70% of Patients

BY BRUCE JANCIN

BERLIN — Omalizumab proved effective and safe in patients with moderate to severe chronic urticaria refractory to antihistamines in a double-blind, placebo-controlled, multicenter trial.

Seventy percent of omalizumab-treated participants were free of all symptoms at 27 weeks, compared with 4.5% of placebo-treated controls.

"For those of you who know urticaria and know how well drugs do in urticaria patients, I think this is absolutely amazing. There's no other drug that can do this. Your favorite antihistamine can't achieve these levels. Plus, these are patients who've already been on pretty much everything else and didn't respond," Dr. Marcus Maurer said at the annual congress of the European Academy of Dermatology and Venereology.

"This is definitely a drug to consider when you have patients who do not respond to your standard urticaria treatment," added Dr. Maurer, a dermatologist at Charité University Hospital, Berlin.

Omalizumab (Xolair, Genentech/Novartis) is a monoclonal antibody directed against IgE that is approved for treatment of severe allergic asthma. It binds to IgE, preventing it from binding to the IgE receptor on mast cells.

For their proof-of-concept study, Dr. Maurer and coworkers restricted eligibility to patients with one specific subtype of urticaria, autoallergic. These are patients with IgE antibodies directed to thyroid peroxidase as an autoantigen.

A total of 27 patients were randomized to omalizumab and 22 to placebo. Two subjects in the omalizumab arm dropped out during the study period, as did five in the control group, mainly due to lack of response.

Mean baseline score on an urticaria assessment scale was 25 out of a possible 42. At 6 months the score in the omalizumab group had dropped to 6, while remaining unchanged in the control group. The omalizumab group also made significantly less use of rescue antihistamines.

Response to omalizumab occurred rapidly, within the first several weeks. "It's very different from asthma patients, who take a couple of months to respond," Dr. Maurer said.

There were no omalizumab-related safety issues. "We know that anti-IgE has a very good safety profile from the thousands of asthma patients treated with this drug," he said.

Xolair is indicated in the United States for treating adults and adolescents aged 12 years and older with moderate to severe persistent asthma. In 2007, the Food and Drug Administration added a black box warning to Xolair, stating that patients must receive injections under direct medical supervision in a health care setting so they can be monitored for signs of anaphylaxis. Anaphylaxis has presented as bronchospasm, hypotension, syncope, urticaria, and angioedema of the throat or tongue in patients receiving as little as one dose of the drug.

'This is definitely a drug to consider when you have patients who do not respond' to standard treatment.

DR. MAURER

Dr. Maurer laid out the patient numbers that make pursuing an indication for omalizumab in urticaria an attractive proposition. The prevalence of urticaria in Europe is estimated at 1.3%, or more than 10 million individuals. Three-quarters of them have chronic spontaneous urticaria and one-quarter have inducible urticaria. The only drugs licensed for the treatment of urticaria are antihistamines, and an estimated 5.7 million Europeans with urticaria are not adequately controlled on those medications.

"Anything else that's second-, third-, or fourth-line is not licensed for treatment of urticaria patients, so we're in desperate need of new therapies for patients who are resistant to nonsedating antihistamines," he said.

Questions that remain to be answered before omalizumab can earn an indication for urticaria include its efficacy in types other than autoallergic urticaria, the drug's mechanism of action, and optimal dosing.

Anecdotally, Dr. Maurer said that he and his colleagues have successfully treated patients with antihistamine-refractory spontaneous urticaria, cold urticaria, physical urticaria, cholinergic urticaria, solar urticaria, pressure urticaria, and other forms of the disease.

Audience members were quick to ask about the cost, which is high.

"It's about 500 euro [about $750] per injection, and these patients typically need one or two injections per month," he replied. "But remember, these patients suffer tremendously, they miss work, and the other drugs are not cheap either."

In a congress highlights lecture devoted to new develeopments in skin allergy, Dr. Torsten Zuberbier singled out the omalizumab study, noting that its symptom-free rate of 70% is "fascinating."

"Now the biologics are coming to dermatological allergy, and we're really going to start to learn more about the mechanisms of our dermatological diseases," observed Dr. Zuberbier, professor of dermatology and head of the allergy branch at Charité University Hospital. He was not involved in Dr. Maurer's study.

The study was funded by Genentech and Novartis. Dr. Maurer has served as a consultant to the companies. ■

More Research Needed

Lichen Planus *from page 1*

meet criteria for full-blown metabolic syndrome, it's also likely their cardiovascular event rate will be somewhat less as well, although this wasn't an end point in the lichen planus study, said Dr. Cohen at the meeting.

The case-control study also identified an intriguing, previously undescribed association between lichen planus and hypothyroidism.

'We're all focusing a lot of energy and research on psoriasis. But we should focus on other diseases as well.'

DR. COHEN

The prevalence of hypothyroidism was 10% in the lichen planus group, compared with 5.7% in controls. The explanation for the link is as yet unclear, but Dr. Cohen indicated that he and his coworkers are eager to follow up on it.

Lichen planus is a common skin disease affecting up to 2% of the population. The finding that it's associated with an increased rate of dyslipidemia, as has previously been established to be the case in psoriasis, raises the question of whether the risk of hyperlipidemia is increased across the board in patients with the other chronic inflammatory papulosquamous skin diseases through some shared but unknown mechanism.

"I've analyzed preliminary data in patients with seborrheic dermatitis or pityriasis rubra pilaris, and I see the same association. But this definitely requires further research," Dr. Cohen said.

"We're all focusing a lot of our energy and research on [the cardiovascular risk of] psoriasis. But we should focus on other diseases as well," he added.

Dr. Cohen didn't report having any relevant conflicts of interest. ■

Ustekinumab Found to Help Improve Sexual Function in Psoriasis Patients

BY BRUCE JANCIN

BERLIN — Impaired sexual function is extremely common in the setting of moderate to severe psoriasis, and ustekinumab therapy reduces these problems by 10-fold.

That's a key quality of life finding from the ongoing randomized double-blind phase III PHOENIX-1 and -2 clinical trials of this human monoclonal antibody directed against the proinflammatory cytokines interkeukin-12 and -23, Dr. Lyn Guenther reported at the annual congress of the European Academy of Dermatology and Venereology.

The marked reduction in sexual difficulties was paralleled by a sharp improvement in overall quality of life in the ustekinumab-treated patients in the PHOENIX studies. Their mean baseline score on the Dermatology Life Quality Index (DLQI) was 12, reflecting a very large negative impact on quality of life. Twelve weeks into the studies, the average DLQI had dropped by 9.1 points for ustekinumab patients, compared with a 0.5-point dip in the placebo arm, according to Dr. Guenther, medical director of the Guenther Dermatology Research Centre and professor of dermatology at the University of Western Ontario, London.

The DLQI is scored on a 0-30 scale. A 5-point or greater improvement is considered clinically significant.

The PHOENIX trials include 1,996 adults with moderate to severe psoriasis who were randomized 2:1 to ustekinumab (Stelara) at 45 mg or 90 mg at weeks 0, 4, 12, and every 12 weeks thereafter or to placebo. After 12 weeks, patients in the placebo group were crossed over to ustekinumab.

The mean age of participants at entry was 46 years. Sixty-nine percent are men. Their average baseline Psoriasis Area and Severity Index (PASI) score was 20, with 26% of their body surface area being affected and an average disease duration of 20 years. Twenty-eight percent had psoriatic arthritis.

Question 9 on the DLQI is designed to explore sexual problems. Here's the phrasing: "Over the last week, how much has your skin caused any sexual difficulties?"

The response options are "not at all," "a little," "a lot," "very much," or "not relevant." A reply of "a lot" or "very much" was interpreted as indicating sexual difficulties.

The prevalence of impaired sexual function by this measure went from 22.4% at baseline—27.1% in women and 20.8% in men—to 2.7% after 12 weeks on ustekinumab. There was no change in the placebo group, but they showed markedly improved overall quality of life and sexual function upon repeat DLQI testing at 24-28 weeks—3 months or more after having been switched to ustekinumab. There was no significant difference between patients on 90 mg as opposed to 45 mg.

The studies are funded by Centocor. Dr. Guenther is a consultant to the company. ■