Omalizumab Effective for Refractory Urticaria

ARTICLES 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.

'For those of you who know urticaria ... there's no other drug that can do this.'

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. "It doesn't seem to matter what type of urticaria you suffer from. The benefit from Xolair is tremendous," he said.

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," Dr. Maurer replied. "But remember, these patients suffer tremendously, they miss work, and the other drugs are not cheap either."

Also in the developmental pipeline are small-molecule IgE inhibitors that are far less expensive to produce than biotech agents and are suitable for oral administration, he noted.

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

Eye Involvement Often Overlooked in Rosacea

BUDAPEST, HUNGARY — Ocular involvement in rosacea is common, yet frequently goes undiagnosed.

Rosacea is one of the most common skin diseases, affecting an estimated 14 million Americans. Some 30%-60% of patients have ocular involvement in addition to the classic chronic central facial erythema, inflammatory lesions, and telangiectasia, Dr. Martin Schaller said at a satellite symposium on advances in translational research in rosacea held in conjunction with the annual meeting of the European Society for Dermatological Research.

Primary care physicians need to have a low threshold for referring rosacea patients with eye symptoms.

DR. SCHALLER

"Often they do not know they have ocular rosacea. Also, the eye doctors they have gone to for 10 years because of ocular dryness, foreign body sensation, or light sensitivity do not know it," observed Dr. Schaller, professor of dermatology at Eberhard Karls University, Tübingen, Germany.

The clinical manifestations of ocular rosacea are blepharitis, conjunctivitis, and, in more severe cases, keratitis. "This is a potentially blinding eye disease," he stressed.

The real diagnostic challenge lies in the fact that 20% of patients with rosacea have ocular symptoms as their first signal of the disease. Their dermatologists and primary care physicians need to have a low threshold for referring their patients with eye symptoms to an ophthalmologist—and not just any ophthalmologist, but one who is experienced with rosacea.

Treatment is oral doxycycline at 100 mg daily or twice daily, tapering to 50 mg daily or every other day, for up to 6 months.

The satellite symposium was sponsored by Galderma Laboratories, LP. ■

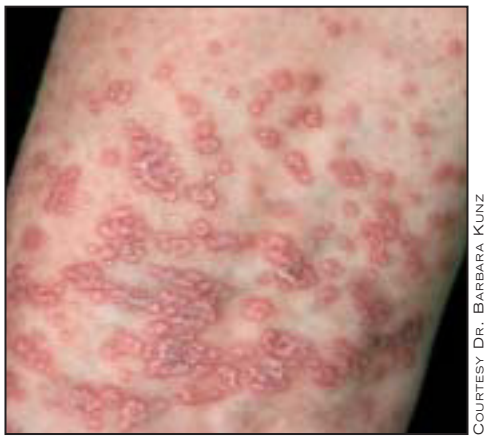
Lichen Planus Linked to Dyslipidemia

BERLIN — Lichen planus, like psoriasis, appears to be intrinsically associated with an increased prevalence of dyslipidemia, according to a large Israeli case-control study.

"Of course, this is a pioneering study and I'd like to see it repeated in other databases. Nevertheless, we suggest that patients with lichen planus might be candidates for dyslipidemia screening," Dr. Arnon D. Cohen said at the annual congress of the European Academy of Dermatology and Venereology.

He and his coinvestigators identified 1,477 patients aged 20-79 years with dermatologist-diagnosed lichen planus in the database of Clalit Health Services, Israel's largest health care organization. They also randomly selected 2,856 controls matched for age and gender, since lichen planus has a female preponderance.

The prevalence of dyslipidemia was 42.5% among the lichen planus patients, significantly greater than the 37.8% figure for controls. After adjusting for potential confounders in a multivariate logistic regression analysis, lichen planus was independently associated with a 34% increased risk of dyslipidemia.



COURTESY DR. BARBARA KUNZ

Lichen planus is a common skin disease affecting up to 2% of the population.

"That's similar to other studies done in psoriasis patients, which have shown increases of about 30% in rates of diabetes and dyslipidemia," observed Dr. Cohen of Ben-Gurion University, Beer-Sheva, Israel.

Unlike what's been found in the psoriasis studies, however, the lichen planus patients did not have higher rates of hypertension, diabetes, obesity, or smoking than did the general population.

Since patients with lichen planus appear to be less likely than those with psoriasis to meet criteria for full-blown metabolic syndrome, it's also likely their cardiovascular event rate will be somewhat less as well, although that wasn't an end point in this study, he said.

Lichen planus is a common skin disease that affects 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. ■