# Omalizumab Effective for Refractory Urticaria

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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.

Of the omalizumab-treated participants, 70% 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 have already been on pretty much everything else and didn't respond," Dr. Marcus Maurer commented 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, of Charité University Hospital, Berlin.

Omalizumab (Xolair) 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 his coworkers restricted eligibility to patients who had 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.

The 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, but the score remained 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.

"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.

**'There's no other drug that can do this. Your favorite antihistamine can't achieve these levels.'**

DR. MAURER

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," Dr. Maurer 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.

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

"This is beautiful. 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," said 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 omalizumab study was funded by Genentech and Novartis, makers of Xolair. Dr. Maurer has served as a consultant to the companies. ■

# *Rupatadine May Reduce Symptoms of 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 antiplatelet-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, said Dr. Metz, of Charité University Hospital, Berlin.

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° C, but while on rupatadine, it dropped to below 4°C, the lowest temperature used 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 moderate headache.

The cause of cold urticaria is unknown. Additional studies comparing the effectiveness of rupatadine and antihistamines lacking PAF-inhibiting action in patients with cold urticaria are needed, Dr. Metz noted.

ACURE was sponsored by Uriach Pharma, which markets rupatadine in Europe, South America, and Africa. The drug is not currently available in the United States. Dr. Metz is a consultant to the company. ■

# Psychiatric Comorbidity Seen In Half of Urticaria Patients

BERLIN — Half of a consecutive series of patients with severe chronic spontaneous urticaria proved to have a previously undiagnosed psychiatric disorder in a multidisciplinary prospective study.

The most common psychiatric comorbidities were anxiety disorders, depression, and somatization disorders, Dr. Martin Metz reported at the annual congress of the European Academy of Dermatology and Venereology.

"The patients that show psychosomatic comorbidities also have significantly higher levels of emotional distress, and this is the main driver of poor quality of life in patients with chronic spontaneous urticaria. So we think it is important to identify these patients," said Dr. Metz of Charité University Hospital, Berlin.

He reported on 100 consecutive patients with severe chronic spontaneous urticaria and no known baseline psychiatric disease who were evaluated for underlying causes of the skin disease, including food or drug intolerance, chronic infection, and autoreactive phenomena.

Patients also were evaluated with the Hospital Anxiety and Depression Scale (HADS), the Symptom Check List (SCL-90R), the Screening for Somatoform Symptoms (SOMS), and the Skindex quality of life questionnaires. Psychiatrists followed up on abnormal psychometric test results and made all the formal psychiatric diagnoses following structured psychosomatic interviews.

A total of 28% of patients were found to have underlying chronic infections, 29% had food or drug intolerance, and 21% had autoreactive urticaria. Overall, 50% of patients received a psychiatric diagnosis: 30% were diagnosed with one or more anxiety disorders, 18% with a depressive disorder, and 18% with a somatoform disorder. Agoraphobia was the most common of the anxiety disorders, with 15% of study participants receiving this diagnosis.

**The study is ongoing to see if treatment of the psychiatric disorders improves patients' skin disease.**

DR. METZ

Psychiatric comorbidity appeared to be more common in certain subtypes of chronic spontaneous urticaria, most notably chronic idiopathic urticaria, with a 70% prevalence of psychiatric comorbidity, and autoreactive urticaria, with a 62% comorbidity rate. The patient numbers, however, are too small to make definitive statements, according to Dr. Metz.

Dr. Metz said that he and his multidisciplinary coinvestigators believe psychiatric illness is a trigger rather than a cause of chronic spontaneous urticaria. The study is ongoing in an effort to see if successful treatment of the psychiatric disorders improves patients' skin disease. ■