



Letters

Efficacy of omalizumab in chronic spontaneous urticaria associated with chronic inducible urticaria

The clinical efficacy and safety of omalizumab treatment in chronic spontaneous urticaria (CSU) has been reported in several clinical trials and real-life studies,^{1,2} and multiple mechanisms have been suggested for the therapeutic effects of omalizumab in the treatment of CSU.³

In 10% to 50% of patients, CSU occurs in combination with chronic inducible urticaria (CIndU), primarily symptomatic dermographism (SD) and delayed pressure urticaria (DPU). The diagnosis of CIndU is made on the basis of the patient history and the results of provocation tests, which make use of the relevant stimuli in controlled settings.⁴ The therapeutic goal of CIndU management is to achieve complete symptom control.⁴

Omalizumab selectively binds to human immunoglobulin E (IgE), thus preventing IgE from binding to its high-affinity receptor (FcεRI) and reducing the amount of free IgE. This process affects the immunologic cascade of urticaria on several levels, thus reducing receptor expression and the release of inflammatory mediators.^{3,4}

Omalizumab is not licensed for the treatment of CIndU. However, CIndU comorbidity is believed to be linked to longer CSU duration and more severe CSU.⁵

There is increasing evidence suggesting that omalizumab is effective in patients with CSU plus CIndU. In a retrospective study, 5 patients with CSU plus DPU and 1 patient with CSU plus SD had complete symptom control after the first use of omalizumab.⁶ In another report, a 37-year-old woman with CSU plus DPU and SD experienced complete remission of her urticaria after the first injection of omalizumab.⁶ In addition, a systematic review of 43 trials, including 2 randomized clinical trials and several case series, found that CIndU improved or resolved in most patients with omalizumab. The evidence is strongest for SD, cold urticaria, and solar urticaria.^{6,7}

Treatment of patients with CSU plus CIndU is, therefore, very likely to improve both CSU and CIndU, even in patients in whom CIndU is the dominant form of chronic urticaria.⁷

Although most patients respond well to omalizumab, the response profile is highly variable and unpredictable, with some responding quickly and others responding slowly or not at all.⁶

We aimed to assess the efficacy of omalizumab (300 mg for 4 weeks) in patients with antihistamine-refractory CSU associated with 1 or more CIndUs in the Urticaria Centers of Reference and Excellence (GA²LEN UCARE) in Rio de Janeiro, Brazil.

We retrospectively reviewed the records of 12 patients with CSU plus CIndU who had been treated with 300 mg of omalizumab every 4 weeks. All patients had used 4-fold, standard-dose, second-generation antihistamines (once a day) for at least 4 weeks. Patients

were not taking montelukast or histamine₂-antihistamines during the study.

To assess CSU disease activity and response to omalizumab, we used the Urticaria Activity Score (UAS), a prospective diary-type tool. The UAS7 is based on the once-daily assessment of itch intensity and number of hives during a period of 7 days. It records the number of wheals and the intensity of pruritus on a 4-point scale (range, 0–3), with a minimum and maximum score of 0 and 6 points per day, respectively. Accordingly, UAS7s range from 0 to 42 points. It is the international guideline–recommended reference standard for measuring disease activity in patients with CSU with wheals. As categorized by Stull et al,⁸ UAS7s of 6 or lower and greater than 6 were used to categorize the disease as controlled and not controlled, respectively. CIndU activity was assessed by performing provocation testing according to subtype. Provocation tests were performed for diagnosis and after omalizumab treatment.⁹

Time to symptom improvement was also assessed. Patients whose UAS7 diminished to 6 or lower within the first 4 weeks after the first omalizumab dose were considered fast responders. Omalizumab slow responders were patients with response (UAS7 ≤6) beyond 4 weeks since first administration of omalizumab. After disease control, antihistamine doses were gradually reduced until standard dose (once a day). According to current international guidelines, none of the patients stopped taking antihistamines while receiving omalizumab.

All patients were women between the ages of 23 and 78 years. Patients had the following CIndUs: SD (n = 10), DPU (n = 7), cold urticaria (n = 1), and heat urticaria (n = 1). Before omalizumab, patients presented with UAS7s of 11 to 42 (mean UAS7, 28). After administration of the first dose of omalizumab, 9 patients achieved urticaria control in 24 to 48 hours (UAS7, 0–4). Three patients did not achieve urticaria control after the first omalizumab dose (UAS remained ≥7), only achieving urticaria control after the second omalizumab dose (UAS7, 0). CIndUs also improved, with all patients having negative provocation test results after omalizumab therapy (Fig 1). The slow responders (n = 3) were patients with SD (1), heat urticaria (1), and DPU (1). No patients in this study reported adverse events other than mild injection-site reactions.

Our results add to prior publications, consisting of case series and a systematic review. Although omalizumab treatment appears to work faster and effectively for SD, 1 of our patients presented a slow response. Two randomized clinical trials in patients with SD and cold urticaria did not find a notable difference between 150-mg and 300-mg omalizumab dosing for these CIndUs, indicating that 150 mg might be an appropriate dose for patients with CIndU.¹⁰ Earlier results also indicate that omalizumab up-dosing may be effective in patients with CIndU who do not respond to their initial dose of omalizumab. These results require further investigation.

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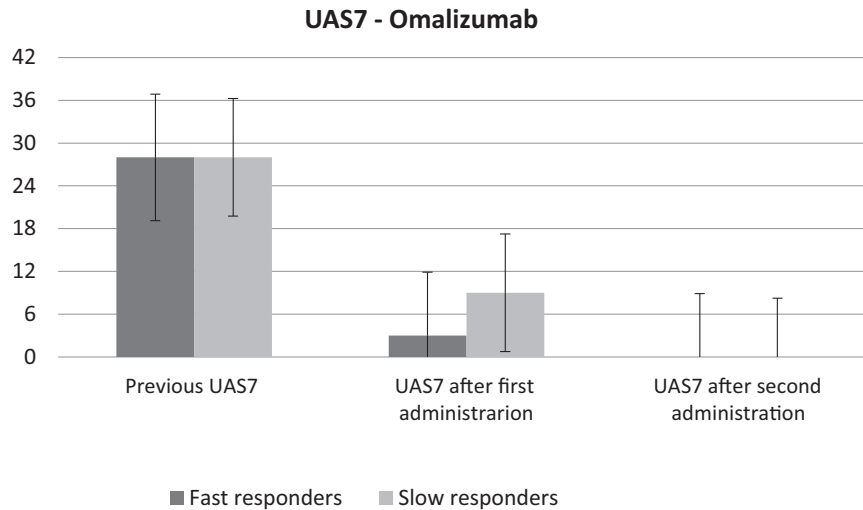


Figure 1. Omalizumab administration and 7-day Urticaria Activity Score (UAS7) range. Error bars indicate the standard deviation.

Randomized controlled trials on the effectiveness of omalizumab in heat urticaria and DPU are lacking, and published evidence is limited. Our study found that omalizumab can be an effective treatment option in heat urticaria and DPU. Despite the small sample, our data corroborate the current literature, which found that omalizumab use in patients with refractory CSU associated with different types of CIndU is effective, allowing symptom control in both CSU and CIndUs.

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