Title Page

Article type: Original article.

Title: Real-life data on the effectiveness and safety of omalizumab in monotherapy or combined for chronic spontaneous urticaria: A retrospective cohort study

Andac Salman¹, Tulin Ergun¹, Ana Maria Gimenez-Arnau²

¹Department of Dermatology, Marmara University School of Medicine, Istanbul, Turkey

²Department of Dermatology, Hospital del Mar, IMIM. Universitat Autònoma. Barcelona, Spain

Corresponding author: Andac Salman, MD

Mailing address: Marmara University School of Medicine, Department of Dermatology, Fevzi

Cakmak Mah, Mimar Sinan Cad. No:41 34899 Pendik, Istanbul, Turkey

Telephone: +902166570606-extension:4649 Fax: +902165970052

ORCID: 0000-0002-6407-926X

E-mail: asalmanitf@gmail.com, andac.salman@marmara.edu.tr

Funding sources: None.

IRB approval status: Reviewed and approved by Marmara University School of Medicine

IRB, (Approval number: 09.2018.233).

Word count (abstract): 200.

Word count (text): 2589.

Figure count: 1.

Table count: 2.

Abstract

Background: The real-life data on the effectiveness and safety of omalizumab in chronic spontaneous urticaria (CSU) with validated methods are scarce. There is also lack of information on the use of combination treatments.

Methods: A retrospective cohort study was done to evaluate the effectiveness and safety of omalizumab in real-life conditions. The patients with CSU treated with omalizumab between 2015 and 2018 were included. The response to therapy was evaluated using urticaria activity score over 7 days (UAS7) and urticaria control test (UCT).

Results: A total of 106 patients were included. A complete response (CR) (UAS7:0) and a well-controlled activity (WCA) (UAS7:1 to <6) were observed in 50 (47.2%) and 35 (33%) patients, respectively. The number of patients with an UCT score ≥ 12 was also significantly increased. Higher rates of CR/WCA were observed with omalizumab monotherapy compared to combination with antihistamines. The combination of dapsone, colchicine and omalizumab provided additional benefit in a small group.

Conclusion: Treatment with omalizumab provided a rapid and sustainable improvement in real-life settings. The use of omalizumab as monotherapy or combined with antihistamines does not show differences in the treatment response. The combination of omalizumab with immunomodulatory agents might be of benefit in selected cases.

Keywords: Chronic spontaneous urticaria, chronic urticaria, omalizumab, real-life.

Introduction

Chronic spontaneous urticaria (CSU) is an inflammatory condition characterized by the persistence of wheals and/or angioedema (AE) for >6 weeks [1]. Various international guidelines recommend omalizumab as a third-line agent for treating CSU [1–3]. The efficacy and safety of omalizumab treatment for CSU has been demonstrated in randomized controlled trials (RCTs) [4–8]. Although RCTs are the gold standard method for evaluating the efficacy and safety of treatment modalities, there is a growing interest for real-life studies. These studies provide information on the effectiveness on the drug in a more heterogeneous group of patients with more reasonable treatment-adherence levels and comorbidities, and over a relatively longer period to evaluate long-term effects and side effects [9,10]. Nevertheless, real-life data on omalizumab treatment for CSU remains scarce and mostly derived from studies lacking standardized treatment protocols and validated methods to measure treatment response. Considering these gaps, this retrospective cohort study aimed to evaluate the effectiveness and safety of omalizumab treatment for CSU in a real-life setting and to identify patient and disease characteristics favoring a favorable treatment response.

Material and Methods

Patients who had been followed up in our specialized urticaria outpatient clinic and had received at least one dose of omalizumab treatment for CSU between 2015 and 2018 were included in the study. The study was reviewed and approved by our institution's ethics committee (Approval number: 09.2018.233).

In our clinic, demographic information and disease characteristics are recorded using a medical chart at the initial visit. The patients with CSU unresponsive ($UCT < 12$ and/or $UAS7 \geq 6$ despite the regular use of nonsedating antihistamines up to four-fold standard dose) antihistamines for ≥ 6 months are administered omalizumab. The treatment is 300 mg every 4 weeks administered subcutaneously. The patients are followed up every 4–8 weeks. If the patient achieves complete remission or shows well-controlled activity, the dosing interval is increased by 1 week at every visit following the first three treatments. In case of a partial response after six injections of omalizumab or any worsening during follow-up, we either add immunomodulatory agents, such as colchicine and dapsone, or increase the omalizumab dose to 450 mg every 4 weeks or combine/switch to treatment with cyclosporine. At every follow-up visit, the severity of the symptoms and disease control are evaluated by the urticaria activity score over 7 days (UAS7) and the urticaria control test (UCT), respectively. The daily UAS score is the sum of daily scores for intensity of pruritus and number of wheals. Thus, the daily UAS scores ranges between 0 and 6, and UAS7 score ranges from 0 to 42 [11]. UCT is a self-reported tool assessing the disease control in patients with CSU, and it provides a final score between 0 and 16 [12]. UCT enables the physician to retrospectively evaluate the disease control and AE symptoms; moreover, it is easy to administer and interpret in clinical practice [12,13].

Medical charts of the patients were reviewed and the patients' gender, age, smoking status, personal history of systemic diseases, atopy, CSU duration, coexisting CIndU/AE, previous

treatments, baseline levels of total immunoglobulin E (IgE), D-Dimer, high-sensitivity C-reactive protein (hsCRP), and erythrocyte sedimentation rate (ESR) were recorded.

Initial dose, frequency, maximum dose interval for omalizumab, concomitant treatments, adverse effects, monthly UAS7, UCT scores were also recorded. Treatment response was recorded as complete response (CR; $\text{UAS7} \leq 0$), well-controlled activity (WCA; $1 < \text{UAS7} \leq 6$), partial response (PR; $\text{UAS7} > 6$, but decreased compared to the baseline, at least 10 points), or no response (NR; no decrease in UAS7). The number of patients with an UCT score ≥ 12 were also analyzed. The patients who responded to treatment were also grouped according to the time to response as fast responders (response ≤ 1 month) or slow responders (response > 1 month).

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) v21.0. Descriptive data are shown as n (%) for categorical variables and mean $\pm$ standard deviation (SD; range) for quantitative variables. The chi-square test was used to compare two categorical variables between independent samples. Student's t-test was used to compare means between two independent groups. Paired samples t-test was used to compare two measurements within the same sample.

Results

A total of 106 patients were included in the study. Patient demographics, disease characteristics, and laboratory tests at the baseline are detailed in Table 1.

At the time of the statistical analysis, 13 (12.2%), 37 (34.9%), 38 (35.8%), and 18 (16.9%) patients were at the first, third, sixth, and twelfth months of omalizumab treatment, respectively.

The initial dose for omalizumab was 300 mg in 103 patients, and only three had received 150 mg. All patients received the treatment every 4 weeks except one; this patient who received 150 mg every 2 weeks initially because of chronic renal failure, and then received 300 mg every 4 weeks. The most common concomitant treatment was antihistamines in 61 (57.5%) patients, whereas in 35 patients (33%) omalizumab was used as a monotherapy. When the omalizumab and antihistamine combination group was compared with the omalizumab monotherapy group, the demographic and baseline disease characteristics (age, gender, duration of disease, previous treatments, baseline UAS7, UCT scores) were similar ($p>0.05$). However, the ratio of the patients showing CR and CR/WCA were significantly higher in the monotherapy group (CR:80% vs 31.1% and CR/WCA:94.3% vs 77%) ($p=0.0001$ and 0.029). A combination of dapsone (150 mg/day) and colchicine (1.5 mg/day) was used in 3 patients in whom the disease was recalcitrant to antihistamines and omalizumab. This combination led to CR in two of them and dapsone, colchicine and antihistamines were gradually discontinued within 4 months. The pre-combination UAS7 scores of 18 and 24 improved to 0 in both patients and the precombination UCT scores of 8 and 10 improved to 16 in both of them following the treatment. They are still on remission with omalizumab treatment every 4 and 8 weeks. The remaining patient did not show any improvement and is being treated with omalizumab 450mg monthly. The treatment characteristics are provided in Table 2.

The mean UAS7 and UCT scores significantly improved every month during the first 6 months of treatment ($p < 0.05$). The mean UAS7 and UCT scores during the treatment were provided in Fig. 1. The number of patients with a UCT score of ≥ 12 was 1 (0.9%), 70 (66%), 73 (78.5%), 53 (94.6%), and 18 (100%) at the baseline, first, third, sixth, and twelfth months of treatment, respectively ($p < 0.001$). Of the 56 patients who had received 6th dose, 32 had CR, 19 had WCA, 4 had PR and one patient had NR. Eighteen patients continued the treatment for one year. Of them 12 had CR, 5 had WCA and 1 had PR. The patient with PR was lost to follow-up, but the CSU was stable in the remaining patients with ongoing treatment. Treatment response at the final visit was detailed in Table 2.

At the time of the final analysis, 73 patients (68.8%) were still receiving omalizumab treatment, whereas 13 (12.2%) were lost to follow-up. Omalizumab was discontinued in 20 patients (19%). The reason was lack of efficacy in ten, remission in eight patients, and adverse effects (exacerbation of urticaria and anxiety) in the remaining two patients (Table 2). Another patient experienced mild bronchospasm following the first injection of omalizumab; however, treatment was continued. At the end of 3 months, a WCA was achieved without any recurrence of bronchospasm. Apart from these, no adverse effects were observed following a total of 729 treatments administered within the study period.

Among the eleven patients who previously responded to omalizumab, retreatment with omalizumab led to CR in six patients and WCA in five.

The subgroup analysis according to gender; age; smoking status; coexisting CIndU or AE; elevated levels of baseline total IgE, D-Dimer, hsCRP, and ESR; response to treatment; and response time did not reveal a statistically significant difference in terms of treatment response, response time, and adverse effects ($p > 0.05$).

Discussion

The present study aimed to determine the real-life effectiveness and safety of omalizumab treatment in a treatment antihistamines resistant CSU cohort. Its results showed a significant improvement, according to UAS7 and UCT scores, without any serious adverse events or long-term toxicity.

The prevalence and incidence of CSU are higher in women [14] and this trend was observed in the present study as well. AE was present in approximately 70% patients, which is higher compared to previous reported data about 16-33% of patients with CSU [15,16]. This discrepancy might be explained because of AE data was collected using a self-reported questionnaire in this study or because our patients had more severe CSU compared to general population studies. The frequency of coexisting CIndU in our study population was 15%, which was reported to be 20-36% in recent studies [16,17]. This might be explained by the fact that the provocation tests were carried out only in patients reporting a physical triggering factor.

The efficacy and safety of omalizumab in patients with CSU have been reported in several RCTs [4–8,18]. Most of these studies have evaluated the treatment response according to changes in UAS7 scores. Baseline UAS7 scores of the patients in these studies ranged between 26.5 and 31.8, which was similar the score of 26 in the present study, indicating severe disease. In our study, the mean change in UAS7 score compared to baseline was –17.2, –20.7, –22 and –22 in the first, third, sixth, and twelfth months of treatment, respectively. Consistent with our results, Saini *et al.* reported 13 points of decrease in UAS7 score following 1 month of treatment [4]. Similarly, the previous phase-III studies reported UAS7 score decreases ranging from 12.1 to 20.7 at the third month of treatment [6,7,18]. The treatment was found to be safe in the earlier studies, with only 0%–4.4% patients discontinuing because of adverse effects (exacerbation of urticaria and anxiety) [4,6,7,18]. In

line with these data, only two patients (1.8%) discontinued the treatment because of adverse effects in our study. Taken together, these data confirm the effectiveness and safety of omalizumab in real-life use which is comparable to clinical studies.

Most of the real-life studies on omalizumab in CSU have limitations because of their retrospective and multicentric design. In previous studies, omalizumab administered at doses of 150 or 300 mg resulted in complete or significant/satisfactory improvement in 66%–88% patients [19–23]. In line with these studies, we observed a CR or a WCA in 80% of our patients.

Unlike these studies, standardized treatment response evaluation methods and treatment protocols were used in our study. We observed a decrease in mean UAS7 score from 26 at baseline to 8.8 and 4.8 at the first and third months of treatment, respectively. These results are consistent with those of other studies reporting a decrease in UAS and UAS7 scores following omalizumab treatment [19,24–26].

This study is in support with the use of UCT as an indicator of disease control with omalizumab [27]. UCT was recently developed to assess the disease control and aid treatment decisions patients with CSU. It also evaluates the symptoms associated with AE [12]. Besides, the changes in UCT scores strongly correlate with the changes in the chronic urticaria-specific quality-of-life questionnaires [28]. UCT scores of ≥ 12 and 16 indicate a good disease control and full control of symptoms, respectively [12,29]. In our study, the number of the patients with a UCT score of ≥ 12 increased continuously during the study period. Moreover, the rate of the patients with a UCT score of 16 improved from 0% to 31.2% and 55.6% at the third and twelfth months, respectively. A recent study reported that minimal clinically important difference of UCT was three points [28]. In the present study, the change in UCT score from baseline to first month was -5.8 , indicating a rapid and effective disease

control with omalizumab. These results, along with those from previous studies, further confirm the effectiveness and safety of omalizumab in real-life settings.

An earlier study has shown that continuing treatment with omalizumab up to 24 weeks led to CR in patients who failed to achieve a CR at 12 weeks [30]. Moreover, extending the treatment up to 6 months was reported to offer added benefit in partial responders [31]. The statistically significant improvement in UAS7 scores up to sixth month in our study supports these data. However, the current study failed to find any predictors of early treatment response, unlike a previous study reporting an association between serum autoreactivity and slow response to omalizumab [32].

Some previous studies investigating the clinical and laboratory predictors of response to omalizumab have reported a better response to omalizumab in patients with negative serum autoreactivity; more recently, better response was correlated with higher baseline serum IgE and D-Dimer levels [33–36]. However, the present study was unable to reproduce those findings. A possible explanation for our results may be the small number of patients with baseline laboratory test results.

Omalizumab was administered as either an add-on treatment along with antihistamines or monotherapy. Although not systematically recorded, in most of the patients using antihistamines as a concomitant treatment, the need for the antihistamines decreased compared to baseline, as was previously reported in a study [26]. The CR rates in the patients without any concomitant treatment were significantly higher than the patients concomitantly treated with antihistamines. These results confirm the different mechanism of action of omalizumab and antihistamine being the therapeutic response independent of each other. Although, these results can simply be explained with the patients showing CR/WAC do not need regular use of antiH1, we could ask ourselves if maintaining the use of antiH1 is necessary during the treatment with omalizumab. In the future, studies comparing the

effectiveness of omalizumab monotherapy to the omalizumab add-on treatment along with antihistamines are warranted.

Another new aspect of this study was the combined use of dapsone and colchicine with omalizumab and antihistamines. The combination was well tolerated and led to CR in 2 of 3 patients. Following the remission dapsone, colchicine and antihistamines were gradually discontinued, and the remission was maintained with omalizumab monotherapy. We believe that in case of partial response to omalizumab, combination treatment with immunomodulatory drugs might be a safe and effective treatment option in addition to omalizumab up dosing. The future studies on the efficacy of different combinations in partial responders to omalizumab might be of interest.

Although the study population was small to draw definite conclusions, retreatment with omalizumab led to CR or WCA in all 11 patients who previously responded well to omalizumab. These results are similar to those observed in an previous study [37], further confirming that the effectiveness and safety of omalizumab are maintained in subsequent retreatment cycles.

Our study has some limitations. First is the lack of information on the relapse rates of the patients in whom the treatment was stopped because of remission. Second, the current study was not specifically designed to evaluate if any laboratory tests correlated with treatment response. Regardless, the small number of patients with baseline laboratory tests and the lack of serial laboratory examinations to assess if test parameters change parallel to treatment response are limitations. Third, there is not a systematic approach to the need for concomitant medication. But, the concomitant use of the UAS7 and the UCT to assess the treatment response and disease control of CSU patients in real-life clinical settings provides valuable information. In our experience, we think that omalizumab treatment in CSU provides rapid relief of symptoms and high levels of patient satisfaction, with sustainable effectiveness

during prolonged treatment. We believe that prospective studies focusing on the clinical and laboratory biomarkers of treatment response, the effects of omalizumab up dosing, the optimal treatment duration and the post-treatment course of the CSU are warranted.

Acknowledgments

None.

Disclosure of interest

Andac Salman has served as a medical advisor and speaker for Novartis. Tulin Ergun has served on the advisory board for Pfizer, received grants for research from Pfizer, carried out clinical trials for AbbVie and Pfizer, received speaking, consulting and congress participation fees from Novartis, Schering-Plough, AbbVie, Merck-Serono, Pfizer and Janssen-Cilag. Ana M. Gimenez-Arnau has served as a medical advisor for Uriach Pharma, Genentech, Novartis, FAES, and GSK, and received research grants supported by Uriach Pharma, Novartis, grants from Instituto Carlos III-FEDER, and waived educational activities for Uriach Pharma, Novartis, Genentech, Menarini, LEO-PHARMA, GSK, MSD, and Almirall.

References

- 1 Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. *Allergy*. 2018;73:1393–414.
- 2 Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol*. 2013;133:1270–1277.e66.
- 3 Beck LA, Bernstein JA, Maurer M. A review of international recommendations for the diagnosis and management of chronic urticaria. *Acta Derm Venereol*. 2017;97:149–58.
- 4 Saini S, Rosen KE, Hsieh H-J, et al. A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J Allergy Clin Immunol*. 2011;128:567–573.e1.
- 5 Maurer M, Rosén K, Hsieh H-J, et al. Omalizumab for the Treatment of Chronic Idiopathic or Spontaneous Urticaria. *N Engl J Med*. 2013;368:924–35.
- 6 Kaplan A, Ledford D, Ashby M, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. *J Allergy Clin Immunol*. 2013;132:101–9.
- 7 Saini SS, Bindslev-Jensen C, Maurer M, et al. Efficacy and Safety of Omalizumab in Patients with Chronic Idiopathic/Spontaneous Urticaria who Remain Symptomatic on H 1 Antihistamines: A Randomized, Placebo-Controlled Study. *J Invest Dermatol*. 2015;135:67–75.
- 8 Staubach P, Metz M, Chapman-Rothe N, et al. Effect of omalizumab on angioedema in H₁-antihistamine-resistant chronic spontaneous urticaria patients: results from X-ACT, a randomized controlled trial. *Allergy*. 2016;71:1135–44.
- 9 Garrison LP, Neumann PJ, Erickson P, et al. Using Real-World Data for Coverage and Payment Decisions: The ISPOR Real-World Data Task Force Report. *Value Health*.

- 2007;10:326–35.
- 10 Saturni S, Bellini F, Braidò F, et al. Randomized controlled trials and real life studies. Approaches and methodologies: a clinical point of view. *Pulm Pharmacol Ther*. 2014;27:129–38.
 - 11 Młynek A, Zalewska-Janowska A, Martus P, et al. How to assess disease activity in patients with chronic urticaria? *Allergy*. 2008;63:777–80.
 - 12 Weller K, Groffik A, Church MK, et al. Development and validation of the Urticaria Control Test: A patient-reported outcome instrument for assessing urticaria control. *J Allergy Clin Immunol*. 2014;133:1365–1372.e6.
 - 13 Kocatürk Göncü E, Aktan Ş, Atakan N, et al. The Turkish Guideline for the Diagnosis and Management of Urticaria-2016. *TURKDERM*. 2016;50:82–98.
 - 14 Lapi F, Cassano N, Pegoraro V, et al. Epidemiology of chronic spontaneous urticaria: results from a nationwide, population-based study in Italy. *Br J Dermatol*. 2016;174:996–1004.
 - 15 Zuberbier T, Balke M, Worm M, et al. Epidemiology of urticaria: a representative cross-sectional population survey. *Clin Exp Dermatol*. 2010;35:869–73.
 - 16 Curto-Barredo L, Archilla LR, Vives GR, et al. Clinical Features of Chronic Spontaneous Urticaria that Predict Disease Prognosis and Refractoriness to Standard Treatment. *Acta Derm Venereol*. 2018;98:641–7.
 - 17 Sánchez J, Amaya E, Acevedo A, et al. Prevalence of Inducible Urticaria in Patients with Chronic Spontaneous Urticaria: Associated Risk Factors. *J Allergy Clin Immunol Pract* 2017;5:464–70.
 - 18 Hide M, Park HS, Igarashi A, et al. Efficacy and safety of omalizumab in Japanese and Korean patients with refractory chronic spontaneous urticaria. *J Dermatol Sci*. 2017;87:70–8.

- 19 Labrador-Horrillo M, Valero A, Velasco M, et al. Efficacy of omalizumab in chronic spontaneous urticaria refractory to conventional therapy: analysis of 110 patients in real-life practice. *Expert Opin Biol Ther.* 2013;13:1225–8.
- 20 Rottem M, Segal R, Kivity S, et al. Omalizumab Therapy for Chronic Spontaneous Urticaria : The Israeli Experience. *Isr Med Assoc J.* 2014;16:487–90.
- 21 Ghazanfar MN, Sand C, Thomsen SF. Effectiveness and safety of omalizumab in chronic spontaneous or inducible urticaria: evaluation of 154 patients. *Br J Dermatol.* 2016;175:404–6.
- 22 Ensina LF, Valle SOR, Juliani AP, et al. Omalizumab in Chronic Spontaneous Urticaria: A Brazilian Real-Life Experience. *Int Arch Allergy Immunol.* 2016;169:121–4.
- 23 Clark JJ, Secrest AM, Hull CM, et al. The effect of omalizumab dosing and frequency in chronic idiopathic urticaria: Retrospective chart review. *J Am Acad Dermatol.* 2016;74:1274–6.
- 24 Giménez-Arnau A, Velasco M, Armario Hita JC, et al. Omalizumab: What benefits should we expect? *Eur J Dermatol.* 2016;26:340–4.
- 25 Vadasz Z, Tal Y, Rotem M, et al. Omalizumab for severe chronic spontaneous urticaria: Real-life experiences of 280 patients. *J Allergy Clin Immunol Pract.* 2017;5:1743–5.
- 26 Türk M, Yılmaz İ, Bahçecioğlu SN. Treatment and retreatment with omalizumab in chronic spontaneous urticaria: Real life experience with twenty-five patients. *Allergol Int.* 2018;67:85–9.
- 27 Kocaturk E, Deza G, Kızıltac K, et al. Omalizumab up dosing for better disease control in chronic spontaneous urticaria patients. *Int Arch Allergy Immunol.* 2018;177:360–4.
- 28 Ohanyan T, Schoepke N, Bolukbasi B, et al. Responsiveness and minimal important

- difference of the urticaria control test. *J Allergy Clin Immunol.* 2017;140:1710–1713.e11.
- 29 García-Díez I, Curto-Barredo L, Weller K, et al. Cross-Cultural Adaptation of the Urticaria Control Test From German to Castilian Spanish. *Actas Dermosifiliogr.* 2015;106:746–52.
- 30 Kaplan A, Ferrer M, Bernstein JA, et al. Timing and duration of omalizumab response in patients with chronic idiopathic/spontaneous urticaria. *J Allergy Clin Immunol.* 2016;137:474–81.
- 31 Asero R, Canonica GW, Cristaudo A, et al. Critical appraisal of the unmet needs in the treatment of chronic spontaneous urticaria with omalizumab: An Italian perspective. *Curr Opin Allergy Clin Immunol.* 2017;17:453–9.
- 32 Gericke J, Metz M, Ohanyan T, et al. Serum autoreactivity predicts time to response to omalizumab therapy in chronic spontaneous urticaria. *J Allergy Clin Immunol.* 2017;139:1059–1061.e1.
- 33 Palacios T, Stillman L, Borish L, et al. Lack of basophil CD203c-upregulating activity as an immunological marker to predict response to treatment with omalizumab in patients with symptomatic chronic urticaria. *J allergy Clin Immunol Pract.* 2016;4:529–30.
- 34 Deza G, Bertolín-Colilla M, Sánchez S, et al. Basophil FcεRI expression is linked to time to omalizumab response in chronic spontaneous urticaria. *J Allergy Clin Immunol.* 2018. doi:10.1016/j.jaci.2018.02.021.
- 35 Ertas R, Ozyurt K, Atasoy M, et al. The clinical response to omalizumab in chronic spontaneous urticaria patients is linked to and predicted by IgE levels and their change. *Allergy.* 2018;73:705–12.
- 36 Cugno M, Genovese G, Ferrucci S, et al. IgE and D-dimer baseline levels are higher in

responders than non-responders to omalizumab in chronic spontaneous urticaria. Br J Dermatol. 2018. doi:10.1111/bjd.16593.

- 37 Metz M, Ohanyan T, Church MK, et al. Retreatment with omalizumab results in rapid remission in chronic spontaneous and inducible urticaria. JAMA Dermatol. 2014;150:288–90.

Tables

Table 1. Patient demographics, disease characteristics, and laboratory test results at the baseline.

Characteristics				
Gender n (%)	Female	73 (68.9)		
	Male	33 (31.1)		
Mean age (years)	Mean ± SD (range)	42.5 ± 15.6 (15–81)		
Mean duration of the disease (months)	Mean ± SD (range)	49 ± 69.8 (6–360)		
Chronic inducible urticaria n (%)	Absent	90 (85)		
	Cold	2 (1.9)		
	Symptomatic Dermographism	8 (7.5)		
	Delayed pressure	5 (4.7)		
	Cholinergic	1 (0.9)		
Angioedema n (%)	Absent	32 (30.2)		
	Present	74 (69.8)		
Previous treatments n (%)	Antihistamines	106 (100)	Dapsone	4 (3.8)
	Montelukast	17 (16)	Sulfasalazine	2 (1.9)
	Systemic CS	67 (63.2)	Cyclosporin	4 (3.8)
	Omalizumab	11 (10.4)	Methotrexate	1 (0.9)
	Colchicine	8 (7.5)		
Associated systemic diseases n (%)	Hypertension	15 (14)	FMF	1 (0.9)
	Diabetes	7 (6.6)	AS	2 (1.9)
	Hypothyroidism	8 (7.4)	Asthma	7 (6.6)
	Hyperthyroidism	1 (0.9)	Chronic renal failure	1 (0.9)

Smoking n (%)	Yes	66 (62.3)
	No	22 (20.8)
	Missing	18 (16.9)
Mean total IgE (n = 73)	Mean $\pm$ SD (range)	633.1 $\pm$ 2647.4 (0–22032)
Mean D-dimer (n = 48)	Mean $\pm$ SD (range)	0.79.1 $\pm$ 1.1 (0.02–6.6)
Mean hsCRP (n = 52)	Mean $\pm$ SD (range)	6.4 $\pm$ 8 (0.16–37)
Mean ESR (n = 77)	Mean $\pm$ SD (range)	18.5 $\pm$ 13.6 (3–68)

AS: Ankylosing spondylitis, CS: Corticosteroid, ESR: erythrocyte sedimentation rate, FMF: Familial Mediterranean fever, hsCRP: high-sensitivity C-reactive protein, SD: standard deviation.

Accepted Manuscript

Table 2. Characteristics of omalizumab treatment and treatment response.

Characteristics		
Starting dose n (%)	150 mg	3 (2.8)
	300 mg	103 (97.2)
Initial dose interval n (%)	Every 2 weeks	1 (0.9)
	Every 4 weeks	105 (99.1)
Mean number of treatments	Mean $\pm$ SD (range)	6.88 $\pm$ 5.93 (1–36)
Mean duration of follow-up (months)	Mean $\pm$ SD (range)	11.12 $\pm$ 12.71 (2–72)
Concomitant treatments n (%)	None	35 (33)
	Antihistamines	61 (57.5)
	Colchicine + antihistamines	7 (6.6)
	Dapsone + colchicine + antihistamines	3 (2.8)
Maximum dose interval (weeks)	Mean $\pm$ SD (range)	5 $\pm$ 1.4 (4–8)
Response time in patients with complete response or well-controlled activity n (%) (n = 85)	Fast	63 (74.1)
	Slow	22 (25.9)
Adverse effects n (%)	None reported	99 (93.4)
	Exacerbation of urticaria	3 (2.8)
	Hair loss	1 (0.9)
	Anxiety	1 (0.9)
	Bronchospasm	1 (0.9)
	Headache	1 (0.9)
Final status of treatment n (%)	On treatment	73 (68.9)
	Off treatment	20 (18.9)
	Lost to follow-up	13 (12.3)
Reason for discontinuation n (%) (n = 20)	Remission	8 (40)
	Inefficacy	10 (50)
	Adverse effects	2 (10)
Treatment response at the final visit n (%)	Complete response	50 (47.2)
	Well-controlled activity	35 (33)
	Partial response	10 (9.4)
	No response	11 (10.4)

SD: standard deviation.

Figure caption

Figure 1. The mean UAS7 and UCT scores (a); and the change in the scores during study period (b). (Paired samples t-test, UAS7: urticaria activity score over 7 days, UCT: urticaria control test)

Accepted Manuscript