

Accepted Manuscript

Efficacy and rapid activity of omalizumab retreatments in chronic spontaneous urticaria

Eustachio Nettis, MD, Elisabetta Di Leo, MD, PhD, Caterina Foti, Prof, Luca Cegolon, MD, MSc, PhD, Angelo Vacca, Prof



PII: S0190-9622(17)32746-9

DOI: [10.1016/j.jaad.2017.11.047](https://doi.org/10.1016/j.jaad.2017.11.047)

Reference: YMJD 12151

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 24 August 2017

Revised Date: 15 November 2017

Accepted Date: 18 November 2017

Please cite this article as: Nettis E, Di Leo E, Foti C, Cegolon L, Vacca A, Efficacy and rapid activity of omalizumab retreatments in chronic spontaneous urticaria, *Journal of the American Academy of Dermatology* (2018), doi: 10.1016/j.jaad.2017.11.047.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Article type: Research letter

Title: Efficacy and rapid activity of omalizumab retreatments in chronic spontaneous urticaria

Eustachio Nettis¹, MD; Elisabetta Di Leo², MD, PhD.; Caterina Foti³, Prof., Luca Cegolon⁴, MD, MSc, PhD; Angelo Vacca¹, Prof.

¹ Department of Biomedical Sciences and Human Oncology Unit of Internal Medicine “G. Baccelli” “Aldo Moro” University of Bari Medical School, Policlinico, Bari, Italy.

² Section of Allergy and Clinical Immunology, Unit of Internal Medicine—“F. Miulli” Hospital, Acquaviva delle Fonti, Bari, Italy

³ Department of Biomedical Science and Human Oncology, Dermatological Clinic, University of Bari, 70124, Bari, Italy

⁴ Scientific Directorate, IRCCS Burlo Garofolo, Trieste, Italy

Corresponding author:

Elisabetta Di Leo, MD, PhD

Section of Allergy and Clinical Immunology, Unit of Internal Medicine

“F. Miulli” Hospital

Strada Provinciale per Santeramo Km 4.100

Acquaviva delle Fonti, Bari, Italy

Tel.: +39 3921037176

E-mail: elisabettadileo71@libero.it

Funding sources: None

IRB approval status: Reviewed and approved by the ethics committee of Bari University Hospital.

Conflicts of Interest:

Eustachio Nettis has received personal fees from Almirall, Bayer and Novartis. All other authors state that they have nothing to declare.

Manuscript word count: 509 words [excluding capsule summary, abstract, references, figures, and tables]

References: 5

Figures: 1

Supplementary figures: 0

Tables: 1

Supplementary tables: 0

Keywords: omalizumab; urticaria; retreatment

The manuscript has not been published previously in print/ electronic format or in another language the manuscript is not under consideration by another publication or electronic media.

To the Editor:

The efficacy and safety of omalizumab for the adjunctive treatment of chronic spontaneous urticaria (CSU) is well documented.¹⁻⁴ However, many patients experience disease flare-ups at variable intervals after the last omalizumab dose and appropriate management of these patients remains unclear.

Our retrospective study included 31 patients with refractory CSU (Table I) who had achieved a complete response to a first course of omalizumab (i.e. $\geq 90\%$ improvement in symptoms)² and then received omalizumab retreatment after disease relapse. A third treatment course was administered to 16 patients who had a complete response to the second round of omalizumab. All patients were treated between September 2015 and July 2017. The study protocol was approved by the ethics committee of Bari University Hospital; informed consent was obtained from all participants.

Based on local labeling information⁵, subcutaneous omalizumab 300 mg was given every 4 weeks for 24 weeks (first treatment course) and was administered again (second and third treatment course) at least 8 weeks after the end of the previous course, to the patients with a UAS7 score similar to that in the pre-treatment stage.

After the first treatment course, all patients obtained a complete response and experienced a relapse of disease with an intensity of symptoms similar to the pre-treatment period within 5 to 20 weeks since their last omalizumab injection (Figure 1).

The rate of complete response after the second course of omalizumab was 93.5% (=29/31). Of these, 16 patients (55%) had an increase in symptom scores, which returned to baseline values within 5–16 weeks since their last omalizumab injection in the second treatment course (Figure 1).

All these patients started on new 24-month course of omalizumab treatment; 15/16 (93.8%) achieved complete remission of symptoms. At the last follow-up, ≥ 8 weeks since the administration of the last dose of omalizumab, 11/15 of these patients (68.7%) had experienced relapse or CSU.

The mean time to achieve complete therapy response was 4.9 weeks in the first treatment course, 3.8 weeks in the second course, and 1.8 weeks in the third, with a statistically significant difference

72 between time to complete response with the first and third course ($p=0.018$). All three omalizumab
73 treatment courses were very well tolerated.

74 Since more of than 90% patients experienced disease relapse after discontinuation of omalizumab³,
75 and considering omalizumab is a very expensive drug, it is rather important to know whether and
76 when these patients can interrupt this medication or whether they have to be retreated in case of
77 recurrence of symptoms after discontinuation of therapy.

78 Despite a relatively small sample size, to the best of our knowledge, this is the first real-life study
79 reporting high safety and efficacy of omalizumab in two subsequent retreatments of relapsed
80 patients indicating that those who achieve a complete response to a first treatment course with
81 omalizumab may have a complete response to subsequent treatment cycles. In two previous
82 studies^{3,4} only one retreatment course was given. In our study, a third treatment course was given to
83 some patients and we found that the response to omalizumab was faster as the number of
84 retreatments increased.

References

1. Zhao ZT, Ji CM, Yu WJ, et al. Omalizumab for the treatment of chronic spontaneous urticaria: A meta-analysis of randomized clinical trials. *J Allergy Clin Immunol.* 2016;137:1742–1750.
2. Metz M, Ohanian T, Church MK, Maurer M. Omalizumab is an effective and rapidly acting therapy in difficult-to-treat chronic urticaria: a retrospective clinical analysis. *J Dermatol Sci.* 2014;73:57–62.
3. Metz M, Ohanian T, Church MK, Maurer M. Retreatment with omalizumab results in rapid remission in chronic spontaneous and inducible urticaria. *JAMA Dermatol.* 2014;150:288–290.
4. Türk M, Yılmaz İ, Bahçecioğlu SN. Treatment and retreatment with omalizumab in chronic spontaneous urticaria: Real life experience with twenty-five patients. *Allergol Int.* 2017 May 26. pii: S1323-8930(17)30057-6 [Epub ahead of print].
5. L'Agenzia Italiana del Farmaco. Piano terapeutico (PT) AIFA per la prescrizione di Xolair (omalizumab) (orticaria cronica spontanea). External link http://www.gazzettaufficiale.it/do/atto/serie_generale/caricaPdf?cdimg=15A0625400100010110001&dgu=2015-08-21&art.dataPubblicazioneGazzetta=2015-08-21&art.codiceRedazionale=15A06254&art.num=1&art.tiposerie=SG

Figure legend

Figure 1. Patients who experienced relapse of disease with an intensity of symptoms similar to the pre-treatment period

112 **Table I.** Patient demographic and clinical characteristics at baseline

	Patients (n=31)
Age, y	48.1±13.4
Female, n (%)	22 (71)
Duration of CSU, months	17.1±10.2
History of angioedema, n (%)	21 (67.7)
CSU medication history, n (%)	
H ₁ antihistamines at the licensed dosage	31 (100)
H ₁ antihistamines at high dosage	11 (35.5)
Leukotriene receptor antagonists	2 (6.5)
Systemic corticosteroids	12 (38.7)
Cyclosporine	1 (3.2)
Total IgE level, KUA/L	
Mean ± SD	131.8±106.6
Median (range)	100 (5-391.2)
Positive thyroid autoantibody test result, n (%)	6 (25.0)
Positive ASST, n (%)	14 (45.2)
In clinic UAS ¹	4.8±0.9
UAS ⁷ ²	23.5±5.7
Weekly ISS ²	13 ±4.3
Weekly no. of hive score ²	10.4±4.2
Presence of angioedema at baseline ² , n (%)	4 (12.9)

113 Values are mean ± standard deviation, or number of patients (%), unless otherwise stated.

114 Abbreviations: ASST: autologous serum skin test; CSU: chronic spontaneous urticaria; ISS: itch
115 severity score; SD, standard deviation; UAS: urticaria activity score.116 ¹Defined as the highest value from the day -14 visit, day -7 visit, and day 1 visit.117 ²Based on data collected in a patient daily diary in the 7 days before the first treatment date.

