Efficacy of omalizumab in severe chronic spontaneous urticaria: real life data from a Greek tertiary center

Running Head: Omalizumab in severe chronic spontaneous urticaria

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Dear Editor,

Patients with chronic spontaneous urticaria (CSU), frequently present poor response to second generation H1 antihistamines and severely impaired quality of life. Despite the recommended up-dosing of H1 antihistamines, many patients remain symptomatic. Omalizumab, a recombinant, humanized anti-immunoglobulin-E antibody, was approved for the treatment of CSU in adults and adolescents, who do not respond to antihistamines (Zuberbier, 2018).

A total of 29 consecutively selected patients with severe and resistant CSU, who were started on omalizumab, were enrolled in this prospective, observational study. Included subjects were aged > 18 years, had severe CSU defined as 7-day Urticaria Activity Score (UAS-7) > 30, and were unresponsive to oral H1-blocking antihistamines at up to four times the licensed dose. Patients with inducible chronic urticaria were excluded.

UAS-7 and concomitant medication score (CMS) were assessed at baseline, at 4, 12, 24 and 36 week. The UAS-7 is a validated tool used to assess urticaria severity. Use of concomitant medications was documented and adjusted at every visit according to the clinical response. CMS was calculated as following: antihistamines (regular dose, 2 points; 4 times the regular dose, 8 points), oral prednisone (<11 mg, 5 points; 11-25 mg, 10 points; >25 mg, 15 points), cyclosporine 3.0 mg/kg daily (8 points), hydroxychloroquine (6 points) and montelukast (2 points). Dermatology Life Quality Index (DLQI) was performed at baseline, at 12 and 36 week.

Patients were treated with subcutaneous omalizumab, at a dose of 300mg every 4 weeks. Even in patients with complete or partial response during the 36 weeks of observation, neither discontinuation nor dose or interval adjustment was tried, since this is our common clinical

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practice. Based on omalizumab responses, outcomes were classified as complete (UAS-7 = 0), partial (UAS-7 = 1 - 28) or no response (UAS-7 = 29 - 42). Adverse events were documented. Ethics board approval and written informed consent were provided.

There was a female predominance in our sample (n = 23). The mean age was 48.65±19.07 years and the median disease duration was 6.0 (2.0-75.0) months. 27.6% (n = 8) of the patients suffered from angioedema. All patients had been previously treated with H1-antihistamines, while 96.6% of the patients had received systemic steroids.

UAS-7, CMS and DLQI were significantly decreased during the weeks of evaluation (Table 1). The proportion of patients who achieved complete remission was 24.1% (n = 7) at week 4 and 72.4% (n = 21) at week 36 (Figure 1). 20.7% (n= 6) of the patients showed improvement but did not achieve complete remission by week 36, while 6.9% (n = 2) of the patients showed no response till week 36. None of the patients had a relapse, after he/she had achieved complete remission. The proportion of patients who required concomitant medication was 89.7% (n = 26) at week 4 and 24.1 (n = 7) at week 36 (Figure 2). No adverse events were reported during the study.

Almost 40% of patients have histamine-releasing IgG autoantibodies against IgE or against the high affinity IgE receptor on mast cells and basophils (Chang, 2015). Omalizumab binds to free IgE, preventing IgE from binding to IgE receptors and thus triggering a down-regulation of FceR1 receptors. Although the exact mechanism is not fully understood, its efficacy has been shown (Bernstein, 2018; Kaplan, 2013; Maurer, 2013; Saini, 2015).

Data on individualization of treatment with dose adjustments or treatment intervals during the long-term management of CSU needs to be further elucidated (Curto-Barredo, 2018; Pinto

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Gouveia, 2017). In our study, treatment with omalizumab achieved control of the disease with a relevant quality of life improvement. However, it is important to follow-up with patients after the end of omalizumab cycles to evaluate the real remission of CSU.

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Table 1: Descriptive statistics for UAS-7, CMS and DLQI during weeks of evaluation

Variables	Baseline	Week 4	Week 12	Week 24	Week 36	P value*
UAS-7 (0-42)						
Mean±SD	41.03±2.24	22.31±16.96	16.90±16.65	5.97±8.89	4.45±9.65	< 0.001
Median (Min-Max)	42.0 (34.0-42.0)	22.0 (0.0-42.0)	12.0 (0.0-42.0)	0.0 (0.0-35)	0.0 (0.0-35)	
CMS (0-39)						
Mean±SD	6.97±4.86	5.72±5.09	3.52±4.04	1.41±2.20	0.90±1.90	< 0.001
Median (Min-Max)	4.0 (2.0-16.0)	4.0 (0.0-14.0)	2.0 (0.0-14.0)	0.0 (0.0-9.0)	0.0 (0.0-6.0)	
DLQI (0-30)						
Mean±SD	27.34±2.59	NA	10.48±11.66	NA	2.69±7.55	< 0.001
Median (Min-Max)	28.0 (22.0-30.0)	NA	7.0 (0.0-30.0)	NA	0.0 (0.0-30.0)	

*Friedman's test; difference across the whole evaluation period

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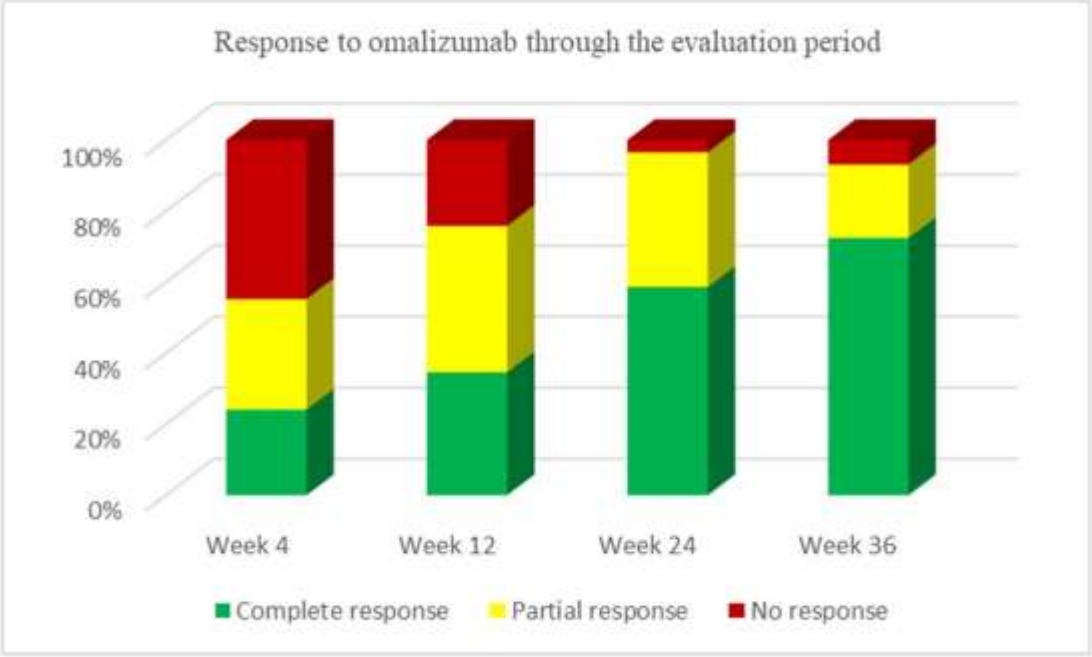
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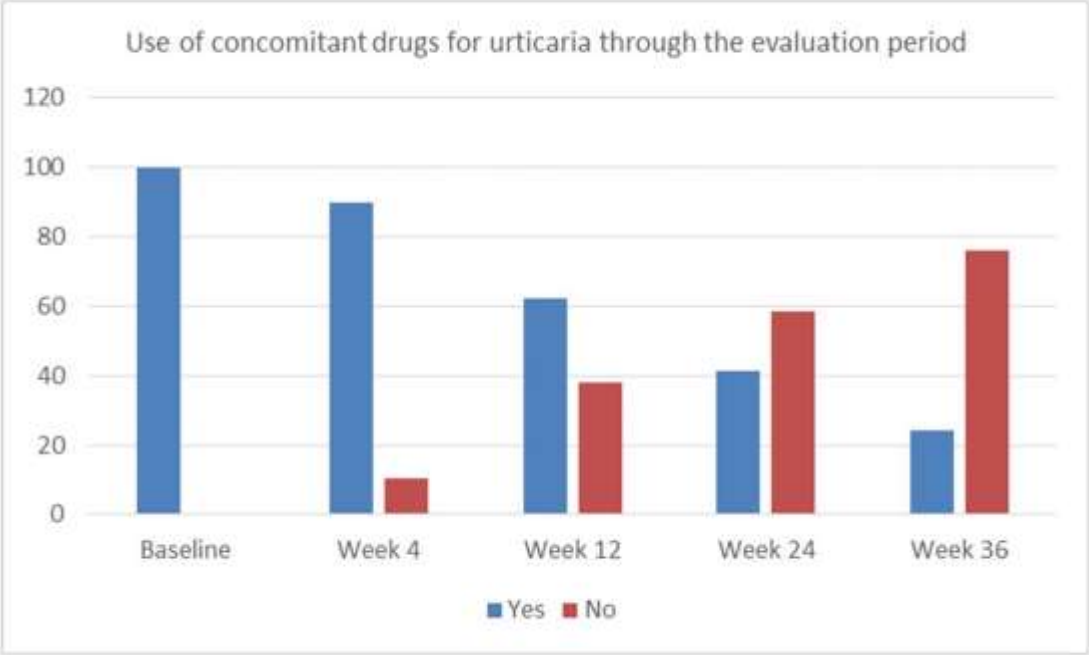
Figure legends

Figure 1: Response rates to omalizumab through the evaluation period

Figure 2: Percentage of patients who required concomitant drugs for urticaria through the evaluation period



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