Omalizumab in children and adolescents with chronic urticaria: A 16 week real-world study

To the editor,

Omalizumab (Xolair®) is a recombinant humanized monoclonal anti-IgE antibody, which binds to free IgE, lowers free IgE levels and causes FcεRI receptors on basophils and mast cells to be downregulated(1). Omalizumab was the first drug approved as an add-on therapy for patients (≥12 years old) with antihistamine-resistant choric urticaria (CU) but not approved for CU in children younger than 12 years(2). The information on the efficacy and safety of omalizumab in the management of pediatric CU is scarce.

We conducted a retrospective, observational real-world study to investigate the efficacy and safety of omalizumab in children and adolescents with antihistamine-resistant CU. Twelve patients aged < 18 years with antihistamine-resistant CU were treated with 150 or 300 mg of omalizumab every four weeks. A summary of the patients' baseline characteristics and dosage regimens are presented in Table 1. We used urticaria control test (UCT) to assess disease control status, children's dermatology life quality index (CDLQI) to evaluate quality of life impairment from baseline to each visit, and monitored adverse events to assess the safety. CU is classified, based on UCT scores, as poorly controlled (<12 points) and well controlled (≥12 points). A CDLQI of 19–30, 13–18, 7–12, 2–6 and 0–1 indicate extremely large, very large, moderate, small and no impairment of patients' QoL, respectively. All 12 patients completed four months of treatment.

Two thirds (67%) of the patients achieved well-controlled CU (defined as a UCT score ≥ 12) after the first administration. The UCT score significantly increased from 2.5 (0.0-5.8) at baseline to 12.0 (1.3-13.8) after four weeks (Z=-3.063, P=0.002) and 15.0 (13.5-16.0) after 16 weeks (Z=-3.065, P=0.002). Patients with well-controlled disease (n= 8) versus poorly controlled disease (n=4) at week four did not differ in

terms of gender, age at onset, disease duration, or IgE levels, UCT scores and QoL impairment at baseline. The CDLQI score decreased from 17.5 (14.5-20.5) at baseline to 9.0 (3.0-13.8) after four weeks (Z=-2.984, P=0.003) and 2.0 (0.0-6.8) after 16 weeks (Z=-3.063, P=0.002). No adverse events were observed. Figure 1 shows UCT and DLQI score at each visit.

Our study confirms the findings of previous case reports(3), i.e. that omalizumab markedly, reliably and quickly reduces CU disease activity and impact in the pediatric age group, which is also similar to what has been described in the adult CU patients(4-6). In line with our findings, a recent review of children with CU younger than 12 years reported that omalizumab achieved a complete response in 81% and a partial response in 19% of patients, without non-responders(7). In our study, omalizumab controlled CU symptoms in children and adolescents rapidly, with two thirds of patients achieving controlled disease after the first administration. The mechanisms of the rapid onset of effects are not entirely understood but are likely to include the reduction of IgE autoantibodies to autoantigens(1). Our study failed to find any predictors of early treatment response as adult patients, i.e., total IgE, BHRA and ASST results, which most likely because of the small number of patients(8).

The study is the first real-world study on omalizumab treatment in children and adolescents with CU. It shows that omalizumab can be used as a highly effective and safe therapeutic strategy for patients with CU aged 3-16 years. The limitations of this study include its small sample size, the relatively short follow-up time and the limited scope of laboratory testing. Also, the UCT is not formally validated for children.

Our clinical experience in 12 children with CU support the current guideline recommendation to switch patients with antihistamine-refractory CU to omalizumab treatment, regardless of their age, and encourage further studies, with longer treatment duration and follow-up.

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CONFLICTS OF INTEREST

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The rest of the authors declare that they have no relevant conflicts of interest.

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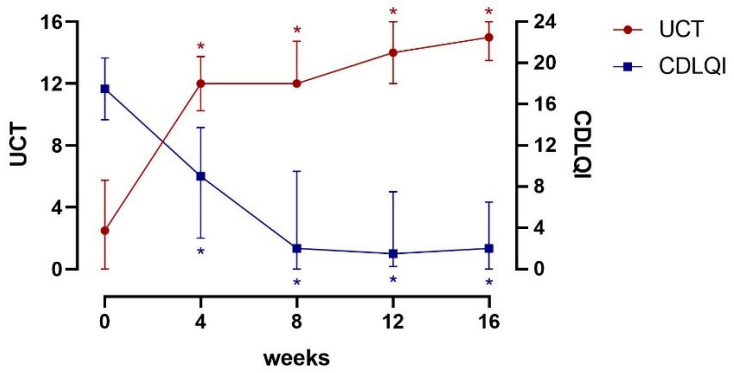
Table 1. Demographic and clinical data of patients including in our study

N	Sex/age (years)	Age at onset (years)	IgE (IU/mL)	ASST	Type of urticaria	UCT	DLQI	Doses, mg/ Interval, weeks
1	F/6	3	1456.2	Positive	CSU+SDerm	5	17	150/4
2	M/5	1	72.6	Negative	CSU	6	12	150/4
3	F/14	11	352.0	Negative	CSU	5	19	150/4
4	F/12	10	106.9	-	CSU	0	24	150/4
5	M/12	11	300.0	Negative	CSU+SDerm +CholU	8	14	150/4
6	M/16	14	34.2	Negative	CSU	7	10	300/4
7	M/3	2	15.2	-	CSU	0	23	150/4
8	F/11	10	821.0	-	SDerm	3	21	150/4
9	F/5	3	98.0	Negative	ColdU	2	17	150/4
10	M/16	15	213.0	Negative	CholU	0	18	300/4→ 150/4
11	F/12	11	498.0	Negative	CSU	0	18	150/4
12	F/10	4	768.0	Negative	Solar urticaria	1	16	150/4
Total: n=12	Total: 7F,5M	Mean±SD: 7.9±5.0	Median (IQR): 256.5(79.0 -700.5)	ASST (+): n=1		Median (IQR): 2.5(0.0-5.8)	Median (IQR): 17.5(14.5-20.5)	

Abbreviations: ASST, autologous serum skin test; UCT, urticaria control test; CDLQI, children's dermatology life quality index; CSU: chronic spontaneous urticaria; SDerm: symptomatic dermographism; CholU: cholinergic urticaria

(A)



(B)

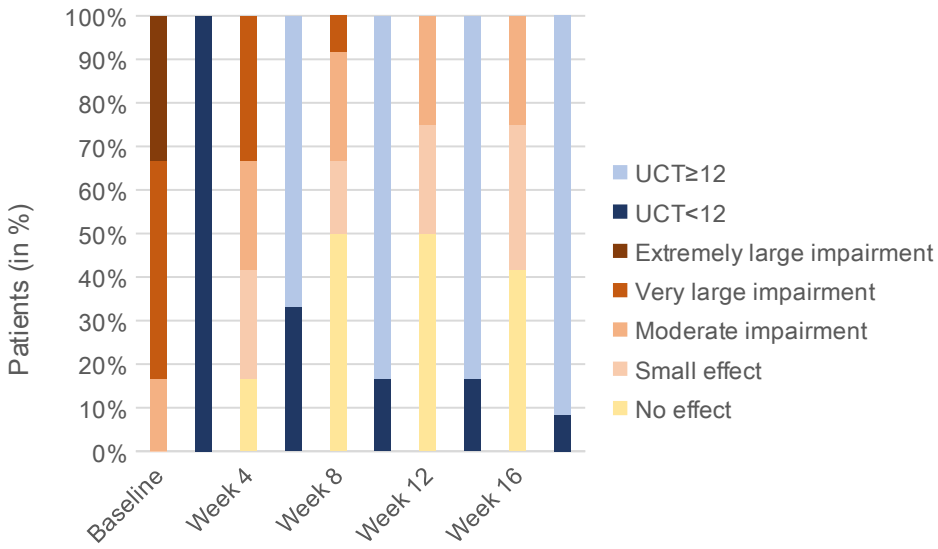


Figure 1 UCT and CDLQI score.

A, The median of UCT and CDLQI at each visit. Data are expressed as interquartile range with median. Applications of omalizumab 150mg or 300 mg every four weeks notably and rapidly improve the disease control and Qol in CU patients as assessed by urticaria control test (UCT) and children's dermatology life quality index (CDLQI). In contrast with baseline, increases in UCT scores and decreases in DLQI scores were significant statistically at each visit (Wilcoxon Matched-Pairs Signed-Ranks Test, $P<0.05$).

B, The proportion of CU patients with poorly controlled (UCT<12) or well controlled (UCT ≥ 12) disease. Twelve patients all completed 16 weeks of omalizumab treatment. Eight patients achieved well controlled at week 4, while three patients at week 8. One case gained a satisfactory response at first and then experienced notable fluctuations, which was exactly the only one whose UCT was 11, below 12.

Abbreviations: UCT, urticaria control test; CDLQI, children's dermatology life quality index; CU, chronic urticaria

*P < 0.05 (Wilcoxon test) compared to week 0.