



Efficacy and safety of omalizumab against chronic spontaneous urticaria: Real-world study from China

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ABSTRACT

Background: Omalizumab is an effective treatment for chronic spontaneous urticaria (CSU) patients aged ≥ 12 years, but its efficacy in patients aged < 12 years has not been fully documented. We evaluated the therapeutic efficacy and safety of omalizumab in Chinese CSU population across all age groups.

Objectives: To assess the efficacy and safety of omalizumab treatment against CSU in China.

Methods: This study was a retrospective and observational study, and the clinical data of CSU patients treated with omalizumab from October 2018 to August 2021 were collected and analyzed.

Results: We enrolled 235 patients in this study, and 54.0% ($n = 127/235$) of patients were female. All patients received at least three injections of omalizumab treatment, and the mean treatment duration was 3.4 ± 1.0 months. At the end of week-12, 98.7% ($n = 232/235$) of patients responded to omalizumab, among which 91.1% ($n = 214/235$) achieved a complete response (CR). An excellent response to omalizumab treatment was observed across all ages. All patients aged < 12 years ($n = 26$) achieved a CR at the end of week-12, and clinical improvement was maintained until treatment cessation. Eighty-seven patients received 3-9-month follow-up after the end of treatment, with a mean duration of 5.7 ± 2.0 months, and 17.2% ($n = 15/87$) patients experienced recurrence after discontinuing treatment. No factors associated with therapeutic response and recurrence to omalizumab treatment were found in this study.

Conclusion: Omalizumab is a safe and efficacious therapy for CSU patients, including those aged < 12 years. We recommend addition of omalizumab to the treatment regimen in CSU patients under 12 years of age.

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Keywords: Chronic spontaneous urticaria, Omalizumab, Therapy, Efficacy, Pediatric patients

INTRODUCTION

Chronic spontaneous urticaria (CSU) is an inflammatory disorder of the skin characterized by recurrent wheals, angioedema, and pruritus for more than 6 weeks. It has been reported that more than 80% of CSU patients could recover within 1 year, but >10% of CSU patients had disease lasting more than 5 years, which seriously impaired quality of life (QoL), interfered with routine daily activities, and mental health.¹

The prevalence and clinical features of CSU vary among different ages. A recent meta-analysis indicated that the prevalence of chronic urticaria in patients under 19 years was slightly higher than adults.² In Europe, the prevalence of CSU was 0.75% in pediatric patients, and it was numerically higher in older age groups (aged 7-11 and 12-17 years) as compared with the youngest age group (aged 0-6 years).³ Another research of Korea showed the highest prevalence at 0-9 years and the lowest prevalence at 10-19 years.⁴ Compared with adults, angioedema was less common in children. It was also reported that nearly 5%-24% children with CSU were affected by angioedema, but this rate in adults was up to 67%.^{3,5} In addition, children may show a better response to treatment. A study including 198 children and 772 adults with CSU in Korea revealed that the improvement rates at 6, 12, and 24 months after treatment were 60.6, 77.8, and 89.2% in children and 45.7, 63.2, and 74.6% in adults, respectively.⁶ Another study in China also exhibited 82.1% of response rate to antihistamines treatment in children, meanwhile it was 62.2% in adults.⁷

Second-generation H1 antihistamines (sgAHs) are recommended as first-line treatment for CSU according to the EAACI/GA²LEN/EDF/WAO guidelines.⁸ A four-fold standard or licensed dose can be used if a standard dose is not adequate. However, not all patients respond clearly to the increased dose. One meta-analysis showed that

the rate of response for CSU was 38.6% with the standard dose of AHs and 63.2% with the increased dose.⁹ Some patients continue to require additional treatments other than AHs.

Omalizumab is a monoclonal antibody targeting free immunoglobulin (Ig)E and binding to the FcεRI on mast cells and basophils. Currently, it is the only biological therapy approved for the treatment of antihistamine-resistant CSU patients aged ≥12 years.^{8,10} Previous clinical trials and real-world studies have shown that omalizumab can effectively improve clinical symptoms in CSU.¹¹⁻¹⁴ A recent prospective study and several real-world studies in China showed that omalizumab was also a safe and efficacious therapeutic drug for Chinese patients with CSU.^{15,16} Nevertheless, participants in most clinical trials are adult patients with CSU. The evidence for omalizumab utilization in patients under 12 years of age are still inadequate.

In this investigator-initiated retrospective study, we systematically evaluated the therapeutic effects of omalizumab in Chinese CSU patients and compared the therapeutic effects of omalizumab in different age groups. This study also presented information on drug changes during the treatment of omalizumab and explored the potential predictors of response and relapse. Owing to the lack of coverage by insurance in China, it is difficult for patients to adhere to the treatment guidelines completely. Therefore, in this study, the use of omalizumab was adjusted according to the symptoms of patient.

METHODS

Patients

Medical records of 347 patients treated with omalizumab were surveyed from October 2018 to August 2021. A diagnosis of CSU was established based on medical history and

clinical symptoms according to EAACI/GA²LEN/EDF/WAO guidelines.³ Forty-four patients were excluded from the study because they were diagnosed with other diseases, and 68 patients were excluded because they did not follow the course of treatment (Fig. 1). Before initiation of omalizumab, patients had to be refractory to at least double dose of AHs or could not tolerate the side effect of AHs.

A total of 235 patients diagnosed with CSU formed the study cohort. Patients were divided into 4 groups based on their age in years: 0-11, 12-17, 18-59, and ≥ 60 . Patients were started on 150 or 300 mg of omalizumab administered every 4 weeks and completed at least 3 follow-up visits at an interval of 4 weeks. Besides omalizumab, original regimens were retained upon enrollment and were adjusted according to changes in disease condition.

Data collection

The detailed information for data collection is provided in supplementary files.

Assessment of efficacy and relapse

The Urticaria Activity Score over 7 days (UAS7) was applied to evaluate disease activity and the treatment effect of omalizumab. The Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL),

Dermatology Life Quality Index (DLQI) and Children's Dermatology Life Quality Index (CDLQI) were utilized to assess QoL impairment. The detailed assessment of efficacy and definition of relapse are provided in supplementary files.

Statistical analysis

The detailed procedure of statistical analysis and software are listed in the supplementary files.

RESULTS

Clinical features of enrolled patients

A total of 235 CSU patients formed the study cohort, and 54.0% ($n = 127/235$) of them were female. The mean age of patients was 33.5 ± 15.7 (range: 4-72) years. The mean disease duration was 25.9 ± 33.0 months, assessed as the time from the diagnosis to initiation of omalizumab treatment. The score of UAS7, CU-Q2oL, DLQI and CDLQI was 24.8 ± 8.6 , 40.2 ± 14.0 , 11.6 ± 4.7 and 9.5 ± 4.8 , respectively, upon treatment initiation (Table 1). All patients received at least 3 injections of omalizumab treatment, and the average treatment period was 3.4 ± 1.0 months (Table 1). The medication schedules of omalizumab were shown in Fig. S1. The median level of serum tIgE among 116 patients were 125.0 (IQR:54.1-248.9) kU/L. A total of 71.6% ($n = 83/116$) of cases had

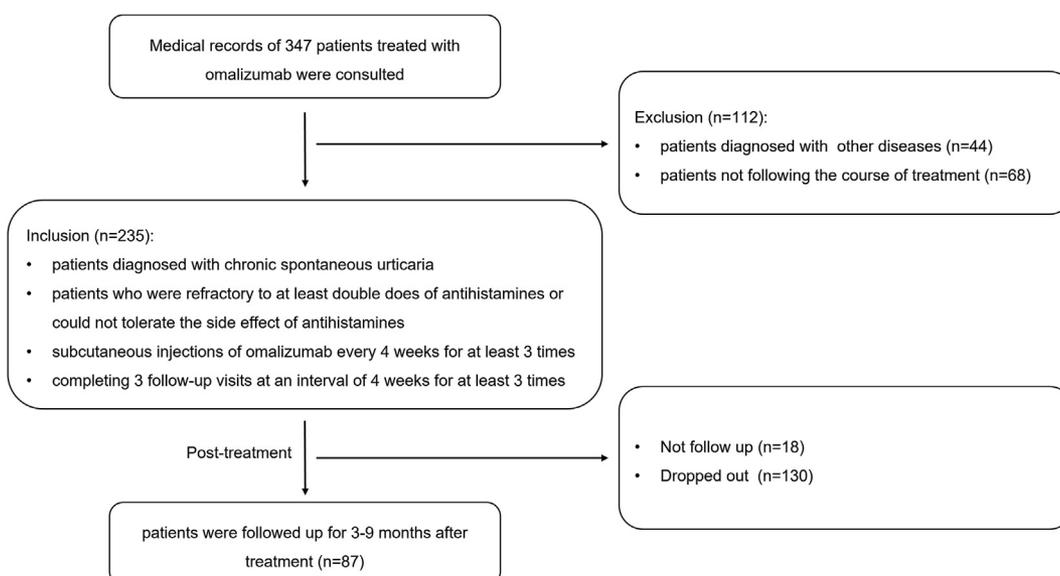


Fig. 1 Study flow chart

Characteristics	Total (n = 235)
Gender, male, n (%)	108 (46.0%)
Ages (year), mean ± SD (range)	33.5 ± 15.7 (4-72)
Disease Duration (month), mean ± SD	25.9 ± 33.0
Baseline of UAS7, mean ± SD	24.8 ± 8.6
Baseline of CU-Q2oL, mean ± SD ^a	40.2 ± 14.0
Baseline of DLQI, mean ± SD ^a	11.6 ± 4.7
Baseline of CDLQI, mean ± SD ^b	9.5 ± 4.8
Treatment period, mean ± SD	3.4 ± 1.0
Total IgE (kU/L), median (IQR) ^c	125.0 (54.1–248.9)
Elevated total IgE, n (%) ^c	76 (65.5%)
ASST positive, n (%) ^d	55 (52.4%)

Table 1. Clinical features of study population. SD: standard deviation; IQR: inter-quartile range; UAS7: Urticaria Activity Score over 7 days; CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; DLQI: Dermatology Life Quality Index; CDLQI: Children's Dermatology Life Quality Index; IgE: immunoglobulin E; ASST: autologous serum skin test. ^aCU-Q2oL and DLQI scores were available for 168 patients aged ≥18 years. ^bCDLQI scores were available for 44 patients aged <18 years. ^cTotal IgE was available for 116 patients. The cut-off value to define a high level of total IgE was >60kU/L. ^dASST test was available for 105 patients

an increased level of serum tIgE (tIgE >60kU/L). ASST was carried out among 105 patients and 52.4% of them (n = 55/105) were positive (Table 1).

We found that 11.1% (n = 26/235) of patients were under 12 years of age, and the mean age was 8.1 ± 2.0 (range: 4-11) years (Table S1). The clinical characteristics and medication regimen were summarized in Table S1 and Fig. S2.

Most patients could benefit from omalizumab treatment

In accordance with other studies, patients showed a rapid response to omalizumab therapy. Within the first 4 weeks of treatment, 96.2% (n = 226/235) of patients achieved a response, and 76.6% (n = 180/235) of them achieved a complete response (CR) (Fig. 2A). At the end of week-12, the proportion of treatment responders had increased to 98.7% (n = 232/235). Among all patients, 91.1% (n = 214/235) showed CR, 7.7% (n = 18/235) showed partial response (PR), and 1.3% (n = 3/235) showed non-response (NR) to omalizumab therapy (Fig. 2A). Consisted with the response to omalizumab, 95.3% (n = 224/235) of patients achieved UAS7 < 7 ("asymptomatic" and "well controlled") at the end of week-12.

Patients across all ages responded well to omalizumab treatment (Table 2). A total of 98.4% (n = 186/189) of patients aged ≥18 years had a response to omalizumab treatment and 89.9% (n = 170/189) achieved CR at the end of week-12. Twenty-six patients aged <12 years also showed an excellent response to omalizumab. A total of 84.6% (n = 22/26) of them achieved a CR at the end of week-4. All patients aged <12 years showed CR at the end of week-8 and maintained it during treatment (Fig. 2B).

Omalizumab improved the clinical symptoms and QoL of patients

A distinct improvement in clinical symptoms and QoL was noted at the end of week-4 and persisted during omalizumab treatment, as assessed by UAS7 and CU-Q2oL scores (Fig. 3, Fig. S3). At the end of week-4, the mean UAS7 score and CU-Q2oL score significantly decreased to 2.5 ± 5.8 (p < 0.0001) and 2.6 ± 7.4 (p < 0.0001) (Fig. 3, Fig. S3). After 12 weeks of treatment, UAS7, CU-Q2oL, DLQI and CDLQI scores decreased to 0.9 ± 3.8 (p < 0.0001), 0.9 ± 4.4 (p < 0.0001), 0.4 ± 1.7 (p < 0.0001) and 0.1 ± 0.5 (p < 0.0001), respectively (Fig. 3, Fig. S3). All clinical scores retained a low-level during the treatment.

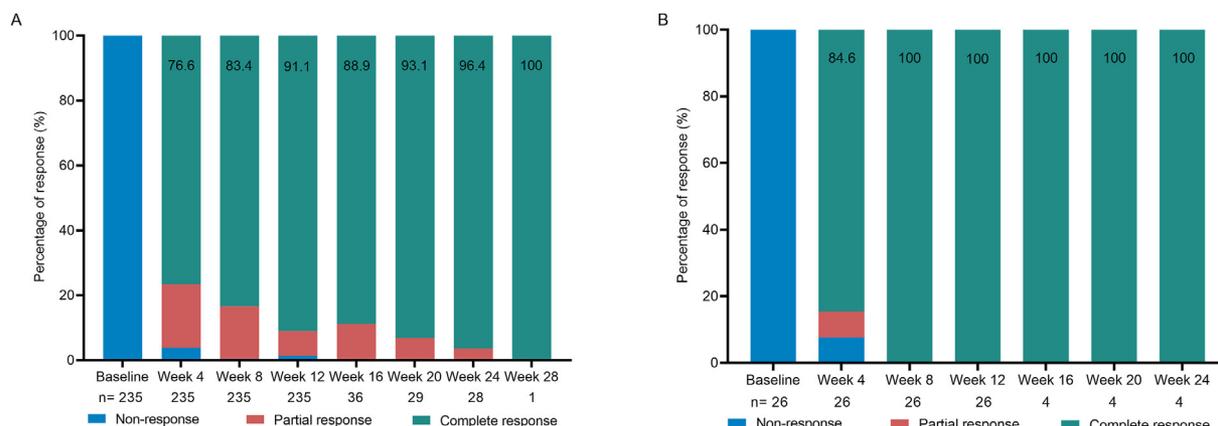


Fig. 2 A. The percentage of patients with non-response, partial response, or complete response during omalizumab treatment. B. The percentage of patients under 12 years of age with non-response, partial response, or complete response during omalizumab treatment.

At the end of week-12, UAS7, CU-Q2oL, DLQI, and CDLQI scores of patients across all ages significantly improved compared with those at the baseline (Table 2). In patients under 12 years of age, UAS7 score fell to 0 at week-8 and were maintained throughout the treatment period (Table 2, Fig. S4).

Responders and non-responders had similar clinical features

Only 1.3% (n = 3/235) of patients did not respond to omalizumab treatment at the end of week-12. There were no significant differences in demographic data, disease duration, or baseline scores of UAS7 between responders and non-responders (Table 3). Differences in immunological

features were also not found. Because there was only 1 available data for non-responders (Table 3), the comparison for IgE could not be applicable between treatment responders and non-responders. The proportion of patients with a positive ASST was similar between responders and non-responders (52.0% vs. 66.7%, p > 0.9999) (Table 3), and the speed of efficacy onset was also concordant between the ASST-positive group and ASST-negative group (p = 0.1754) (Fig. S5).

Omalizumab treatment reduced the drug burden of patients

Before initiating omalizumab treatment, 73.2% (n = 172/235) of patients received double doses of AH, 20.4% (n = 48/235) received AHs and oral

Characteristic	0-11 years (n = 26)	12-17 years (n = 20)	18-59 years (n = 179)	≥ 60 years (n = 10)
UAS7, mean ± SD				
Baseline	20.9 ± 8.9	21.2 ± 8.9	25.9 ± 8.3	21.0 ± 9.1
Week 12	0	0.7 ± 2.0	1.2 ± 4.3	0
CU-Q2oL, mean ± SD ^a				
Baseline	N/A	N/A	40.5 ± 14.1	34.3 ± 10.8
Week 12	N/A	N/A	0.9 ± 4.5	0
CDLQI/DLQI, mean ± SD ^b				
Baseline	9.3 ± 5.0	9.8 ± 4.6	11.6 ± 4.8	10.9 ± 2.7
Week 12	0	0.3 ± 0.8	0.4 ± 1.8	0
Response, n (%)	26 (100%)	20 (100%)	176 (98.3%)	10 (100%)
Drug discontinuation at the end of entire treatment, n (%)	19 (73.1%)	12 (60%)	119 (66.5%)	5 (50%)

Table 2. Treatment outcomes of omalizumab in different age groups. UAS7: Urticaria Activity Score over 7 days; CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; CDLQI: Children’s Dermatology Life Quality Index; DLQI: Dermatology Life Quality Index. ^aCU-Q2oL were available for 168 patients aged ≥18 years. ^bDLQI scores were available for 168 patients aged ≥18 years; CDLQI scores were available for 44 patients aged <18 years

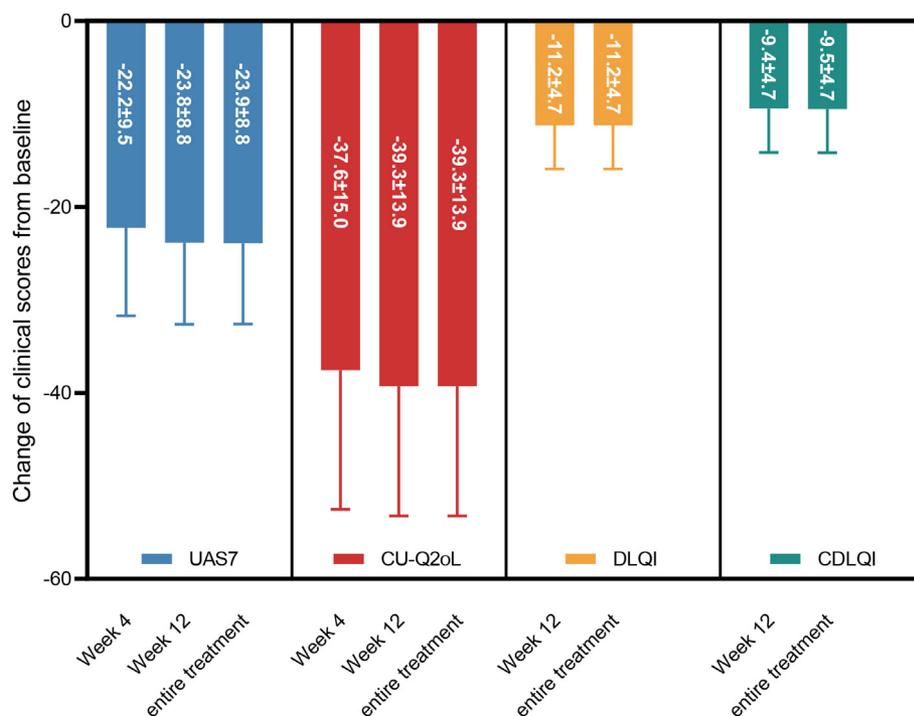


Fig. 3 Change of UAS7, CU-Q2oL, DLQI and CDLQI scores of all patients from baseline during treatment duration. CU-Q2oL and DLQI were available for 168 patients aged ≥ 18 years. CDLQI were available for 44 patients aged < 18 years. UAS7: Urticaria Activity Score over 7 days; CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; DLQI: Dermatology Life Quality Index; CDLQI: Children’s Dermatology Life Quality Index.

glucocorticoid, 2.6% ($n = 6/235$) received AH and immunosuppressant, and 3.0% ($n = 7/235$) received a combination of 3 AHs (Table S2). At the end of omalizumab treatment, the proportion of patients using glucocorticoid decreased to 0.4% ($n = 1/235$, $p < 0.0001$), and no patient received immunosuppressant ($p = 0.0303$) (Table S2). Omalizumab treatment also reduced the use of AHs. The use of double dose AHs and a combination of 3 AHs decreased to 5.1% ($n = 12/235$, $p < 0.0001$) and 0.4% ($n = 1/235$, $p = 0.0680$) at the end of omalizumab treatment, respectively (Table S2). The proportion of patients treated with standard-dose AHs increased to 28.1% ($n = 66/235$, $p < 0.0001$) (Table S2). Notably, a significant proportion of patients discontinued treatments other than omalizumab when therapy started. After the first administration, this proportion was 33.6% ($n = 79/235$, $p < 0.0001$) and increased to 66.0% ($n = 155/235$, $p < 0.0001$) at the end of omalizumab treatment (Table S2).

Among all age groups, a rate of discontinuation of 73.1% ($n = 19/26$) was reported in patients

under 12 years of age, numerically higher than that of other age groups but without statistical difference (Table 2).

Relapse after discontinuation of omalizumab treatment

Up to 92.3% ($n = 217/235$) of CSU patients achieved “UAS7 = 0” at the end of omalizumab therapy. One hundred and thirty patients dropped out when omalizumab treatment finished, and 40.1% ($n = 87/217$) of patients finished a 3–9-month follow-up (Fig. 1). The mean duration of follow-up was 5.7 ± 2.0 months. We found that 82.8% ($n = 72/87$) of patients did not relapse and 17.2% ($n = 15/87$) of patients experienced a relapse during follow-up. None of patients aged < 12 years (17.2%, $n = 15/87$) had a relapse during follow-up, with a mean remission period of 5.4 ± 2.1 months. The mean relapse duration was 5.5 ± 1.9 months. There were no differences among demographic data, disease duration, baseline clinical scores, and laboratory tests between patients who relapsed and those who did not (Table 4).

Characteristics	Responder (n = 232)	Non-responder (n = 3)	P value*
Gender: Female n (%)	126 (54.3%)	1 (33.3%)	0.5953
Age (year), mean ± SD	33.4 ± 15.7	41.0 ± 12.1	0.4030
Disease duration (month), mean ± SD	26.0 ± 33.2	20.0 ± 13.9	0.7949
Baseline of UAS7, mean ± SD	24.7 ± 8.6	32.7 ± 9.0	0.1286
Elevated total IgE, n (%) ^a	76 (66.1%)	1 (100%)	N/A
ASST: positive, n (%) ^b	53 (52.0%)	2 (66.7%)	>0.9999

Table 3. The comparison of clinical features and laboratory tests between responders and non-responders. SD: standard deviation; UAS7: Urticaria Activity Score over 7 days; IgE: immunoglobulin E; ASST: autologous serum skin test. * P value for comparisons between responders and non-responders. ^aTotal IgE was available for 116 patients. The cut-off value to define a high level of total IgE was >60kU/L. As only one data was available for non-responders, statistical analysis was not applicable. ^bASST test was available for 105 patients.

Omalizumab was well tolerated

A total of 84.7% (n = 199/235) of patients discontinued injection of omalizumab at the end of week 12, and the longest treatment duration was 28 weeks. During treatment period, only 2.6% (n = 6/235) of patients reported adverse events (AEs). The most common AE was injection-site reaction, which was reported by 3 patients. Two patients reported body weight gain and increased hair loss, respectively. One patient experienced joint pain. There were no serious AEs.

DISCUSSION

Omalizumab is very efficacious and safe for the treatment of AH-resistant CSU. Several real-world studies have reported a rate of response 87.0–91.4% in CSU patients.^{14,16–21} Consistent with the

previous studies, rapid and effective improvement in clinical scores and QoL were also observed in our study. In our study, 98.7% (n = 232/235) of patients including patients aged <12 years achieved a response at the end of week-12, among which 91.1% (n = 214/235) reached a CR. There are very few studies to systemically evaluate the application of omalizumab in Chinese patients with CSU, especially for patients under 12 years of age.¹⁶ To our knowledge, this study includes the largest cohort of Chinese patients across all ages so far.

The rate of response in our study was much higher in this study than that reported previously. A recent real-world study in China involving 133 adult CU patients treated with omalizumab reported a total response rate of 87.0% and a CR rate of 65.2%.¹⁶ This inconsistency may be due to the differences in the inclusion criteria. Compared

Characteristics	Relapsed (n = 15)	Non-relapsed (n = 72)	P value*
Gender: Female n (%)	7 (46.7%)	42 (58.3%)	0.5683
Age (year), mean ± SD	31.7 ± 15.7	30.0 ± 17.4	0.4637
Disease duration (month), mean ± SD	34.5 ± 47.1	26.8 ± 31.1	0.9517
Baseline of UAS7, mean ± SD	25.8 ± 9.3	22.5 ± 8.9	0.1790
Baseline of CU-Q2oL, mean ± SD ^a	42.1 ± 10.5	35.5 ± 13.3	0.0929
Total IgE (kU/L), median (IQR) ^b	346.0 (25.9–707.3)	129.1 (75.6–231.5)	0.6691
Elevated IgE, n (%) ^b	4 (66.7%)	28 (75.7%)	0.6367
ASST: positive, n (%) ^c	6 (75.0%)	18 (64.3%)	0.6910

Table 4. The comparison of clinical features and laboratory tests between relapsed patients and non-relapsed patients SD: standard deviation; IQR: inter-quartile range; UAS7: Urticaria Activity Score over 7 days; CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; IgE: immunoglobulin E; ASST: autologous serum skin test. *P value for comparisons between relapsed patients and non-relapsed patients. ^aCU-Q2oL scores were available for 54 patients aged ≥18 years. ^bTotal IgE was available for 43 patients. The cut-off value to define a high level of total IgE was >60kU/L. ^cASST test was available for 36 patients.

with other studies that mainly included moderate to severe AH-resistant CU patients, 13.2% (n = 31/235) of patients with mild symptoms (UAS7 <16) were included in this study. The baseline UAS7 score in our study was lower than that of other studies. Furthermore, no patients received four doses of AHs prior to initiation of omalizumab treatment, because receiving such a high dose of AHs is usually challenging for Chinese patients. The mild symptoms and medication history may explain the high response rate noted in our study.

An excellent response to omalizumab treatment in patients under 12 years of age was observed in our study. According to epidemiological studies, the prevalence of chronic urticaria in pediatric patients may be higher than other age groups,^{2,5} whereas the treatment need is not met in patients under 12 years of age. Previous studies have demonstrated that omalizumab may also be an effective therapy in CSU patients under 12 years of age.^{22,23} In this study, all pediatric patients aged <12 years obtained rapid remission after omalizumab treatment, regardless of dose, or administration frequency of omalizumab. In addition, children showed a highest rate of discontinuation across all age groups. These data suggest that omalizumab is an effective treatment for CSU patients under 12 years of age. Treatment with 150 mg omalizumab every 4 weeks was very efficacious in controlling clinical symptoms for children.

It has been suggested that patients with a high level of IgE may respond better to omalizumab treatment.^{17,18,24,25} Moreover, patients with positive ASST may show a slow response to omalizumab treatment in some studies.^{16,26} However, our data do not support the notion that the serum IgE level or positive ASST are predictors of response to omalizumab or the speed of efficacy onset. Another finding is that omalizumab decreased the usage of antihistamines, glucocorticoids and immunosuppressive agents in patients, and more than half of patients discontinued use of other drugs after treatment.

The relapse rate after discontinuation of omalizumab treatment has been reported to be high, ranging from 17.6% to 67.4%.^{11,14,16,27,28} In our study, the relapse rate was 17.2% (n = 15/87), and none of patients under 12 years of age

(n = 15) experienced a relapse during follow-up. No significant differences in clinical features and laboratory tests were found between patients who relapsed and those who did not. The relapse rate was lower compared with that in another study undertaken in China, which reported a relapse rate of 67.4% in adult patients.¹⁶ A possible explanation for this difference is that the symptoms of patients in our study were mild, which resulted in a low relapse rate after discontinuation of omalizumab treatment.

A potential limitation of this study was that the data was collected only from 2 specialist urticaria centers, which may not perfectly represent the clinical characteristics of all CSU patients in China. Moreover, the analysis of predictors of response to omalizumab treatment was limited because there were only 3 patients who did not respond to omalizumab treatment. Another limitation was that the drug cost of using omalizumab treatment was not recorded in detail, making it difficult to calculate the economic benefits to patients.

In conclusion, we enrolled the largest number of CSU patients in China across all ages. Although most patients discontinued treatment of omalizumab after 3 injections, omalizumab appears to be a safe, rapid-acting, and efficacious drug for CSU treatment. Omalizumab treatment showed promising results in patients under 12 years of age. We recommend addition of omalizumab to the treatment regimen in patients under 12 years of age and recommend 150 mg every 4 weeks as the initial dose.

Abbreviations

AEs; adverse events, ASST; autologous serum skin test, CDLQI; Children's Dermatology Life Quality Index, CR; complete response, CSU; chronic spontaneous urticaria, CU-Q2oL; Chronic Urticaria Quality of Life Questionnaire, DLQI; Dermatology Life Quality Index, IgE; immunoglobulin E, IQR; inter-quartile range, NR; non-response, PR; partial response, QoL; quality of life, SD; standard deviation, sgAHs; second-generation H1 antihistamines, UAS7; Urticaria Activity Score over 7 days

Author contributions

A. Wang and Y. Yun performed the study, analyzed the data, and A. Wang wrote the manuscript; Z. Wen, Y. Gao and Q. Shu performed the study; Y. Liang, Y. Zhang, and X. Yao designed and performed the study, coordinated the research, and X. Yao wrote the manuscript.

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Ethics approval

The Ethics Committee of Hospital for Skin Diseases, Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College (Nanjing, China), and Dermatology Hospital, Southern Medical University (Guangzhou, China) approved this study. This study was registered in Chinese Clinical Trial Registry (www.chictr.org.cn, Registration number: ChiCTR2200056599).

Consent for publication

The submission of the article and the publication of the article by World Allergy Organization Journal has been approved by all authors and the responsible authorities at the institution where the work is carried out.

Availability of data and materials

The datasets are available on ResMan (<http://www.medresman.org.cn/uc/index.aspx>).

Submission declaration

All authors have read and approved all versions of the manuscript, its content, and its submission to World Allergy Organization Journal. We confirm that the manuscript is original and has not been considered or published elsewhere.

Declaration of competing interest

X. Yao received speaker's fees from Novartis, Sanofi Regeneron, LEO, Pfizer, and AbbVie. Y. Liang received speaker's fees from Sanofi Regeneron, Lilly, Novartis, and LEO.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.waojou.2022.100719>.

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