Omalizumab for Chinese patients with moderate-to-severe allergic asthma in real-world clinical setting: a prospective, observational study

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ABSTRACT

Background We aimed to investigate the effectiveness of omalizumab, a monoclonal anti-immunoglobulin E antibody, in Chinese patients with moderate-to-severe allergic asthma in real-world clinical practice.

Methods This single-centre, prospective, observational study included Chinese patients aged 14–75 years with moderate-to-severe allergic asthma according to the Global Initiative for Asthma criteria. Omalizumab was administered subcutaneously, and the investigator collected real-world data on exacerbations, steroid exposure, pulmonary function and laboratory assessments at weeks 16, 24, 52, 104 and 156 after treatment initiation. The primary outcome was reduced exacerbations, measured as the proportion of patients with exacerbations in the year following omalizumab initiation. Bowker’s test for paired proportions was performed to compare exacerbation rates before and after treatment initiation. A generalised linear mixed model was used to compare the number of exacerbations.

Results The mean treatment duration was 46.6 weeks for the full analysis set (n=398). The proportion of patients with exacerbations in the year before and after omalizumab initiation was 80.4% (181/225) and 18.7% (42/225) (difference: −61.8%, 95% CI −68.5 to −54.0, p<0.0001), respectively. At week 52, 67.4% of patients discontinued oral corticosteroids, and 19.5% reduced inhaled corticosteroids. The Asthma Control Test scores increased by 4.6 at week 52 from baseline (p<0.001). Forced expiratory volume in 1 s increased by 11.2% and 9.0% at weeks 24 and 52, respectively, from baseline (p<0.01). Injection site reactions (5.2%) were the most frequently reported adverse event.

Conclusions In real-world clinical practice, omalizumab treatment remarkably reduced exacerbations in Chinese patients with moderate-to-severe asthma. Omalizumab reduced the use of oral corticosteroids and improved asthma control and pulmonary function.

INTRODUCTION

Asthma is a heterogeneous disease characterised by chronic airway inflammation and hyper-responsiveness. Low-dose inhaled corticosteroids (ICSs) are effective for mild-to-moderate asthma; however, uncontrolled asthma usually requires higher doses of ICS or long-acting beta-agonists (LABA) and, in some cases, oral corticosteroids (OCS). The prevalence of asthma has been increasing worldwide. In China, an epidemiological study between 2012 and 2015 indicated an overall prevalence of approximately 4.2% among adults. Furthermore, a recent study in China reported that moderate-to-severe asthma was approximately 16% of newly diagnosed cases. Another cross-sectional study in 2020 found that 38.9% of Chinese patients did not achieve satisfactory asthma control.

Previous studies have reported that nearly 90% of patients with severe asthma were cases of allergic asthma, in which IgE plays a critical role. IgE leads to an inflammatory cascade by activating effector cells (eg, mast cells and basophils) through high-(FcεR I) or
low-affinity (FcεRII) receptors. Therefore, targeting IgE to block the inflammatory activity may be an effective therapeutic strategy for treating severe allergic asthma.

Omalizumab, a human anti-IgE monoclonal antibody class medication, competitively binds to circulating IgE and inhibits the binding of IgE to mast cells and basophils, thereby reducing serum IgE levels by approximately 90%. Randomised controlled trials (RCTs) and real-world studies have confirmed the efficacy of omalizumab in improving the management of asthma and reducing exacerbations. Omalizumab is recommended as an add-on therapy to improve asthma control, reduce exacerbations and decrease OCS exposure in patients aged ≥6 years with uncontrolled allergic asthma.

Omalizumab was first introduced to Chinese patients with persistent uncontrolled allergic asthma in Taiwan in 2008. Since 2018, omalizumab has become available in major teaching hospitals across mainland China. The 2018 Global Initiative for Asthma (GINA) guidelines recommend omalizumab as a step 5 add-on therapy for moderate-to-severe asthma on failing step 4. Updated Chinese and international guidelines (1) support the use of omalizumab in clinical practice. The delayed arrival of omalizumab is expected to be effective in Chinese patients with moderate-to-severe asthma by reducing clinically significant exacerbations and ICS or OCS exposure. Because omalizumab is new to clinical practice in China, real-world data generation is scarce. This study investigated the efficacy of omalizumab in Chinese patients with moderate-to-severe allergic asthma in a real-world clinical setting.

METHODS

Study design and setting

This single-centre, prospective, observational study was conducted at a tier-3 teaching hospital (Beijing Chao-Yang Hospital, Affiliated with the Capital Medical University). We recruited patients with moderate-to-severe allergic asthma who initiated omalizumab treatment at a respiratory outpatient specialist clinic between March 2018 and March 2022. Patients were referred from the community medical centre or approached the research clinic directly. Patients received a confirmatory diagnosis of asthma and began specialty care promptly. Moderate asthma was defined as well-controlled asthma according to the treatment outlined in step 3 of the GINA guidelines (ie, low-dose ICS and LABA). Severe asthma was defined as requiring the treatment outlined in step 4 or 5 of the GINA guidelines (ie, high-dose ICS and LABA) to prevent uncontrolled asthma or the progression of uncontrolled asthma despite such treatment.

The study followed routine clinical practice for long-term asthma control per the GINA and Chinese guidelines. The investigators and treating physicians specialising in respiratory medicine assessed the patient, calculated the initial dose of omalizumab, and followed the patient on treatment initiation. The investigators designed the study and analysed the data.

Patient

Patients were eligible if they were Chinese, between 14 and 75 years, and had moderate-to-severe allergic asthma, as defined by the GINA guidelines. Key inclusion criteria were as follows: (1) history of asthmatic symptoms (wheezing, coughing, shortness of breath with or without chest tightness); (2) a positive prick skin test or quantitative serological test (Phadiatop) for allergens (ie, dust mite, cockroach, mould, cat, dog); (3) confirmed variable expiratory airflow limitation assessed according to the GINA guidelines (ie, bronchodilator reversibility test) and (4) symptoms controlled by low-dose or high-dose ICS plus LABA, or poor control despite high-dose ICS plus LABA for at least 3 months.

Patients were excluded if they had a primary diagnosis of respiratory diseases other than asthma (ie, chronic obstructive pulmonary disease, severe pulmonary emphysema, pulmonary fibrosis or sleep apnoea), cardiac insufficiency grade 3 or higher based on the New York Heart Association classification, or obstruction of the larynx or trachea. Pregnant or breastfeeding women and those allergic to omalizumab were also excluded. Patients with comorbidities (ie, obesity or smoking) were included if they met the disease definition without contraindications to omalizumab use.

Study procedure and assessments

A confirmatory diagnosis of allergic asthma was made at the initial clinic visit. The patients underwent an allergen screening (qualitative serological) test and were asked about symptoms and signs (eg, wheezing and coughing). The treating physician performed the pulmonary function test for variable expiratory airflow limitation, laboratory assessments (ie, IgE, eosinophil and fractional (exhaled nitric oxide) for inflammatory activity, and documented any clinically significant exacerbations occurring within 1 year before the clinic visit (including hospitalisation). Antiasthmatic treatments (ICS, LABA and OCS) were reviewed and adjusted based on disease severity assessment. To initiate omalizumab treatment, the treating physician determined the dosage according to the body weight and serum IgE levels of each patient. The clinic nurse, trained in omalizumab administration, prepared and injected the drug subcutaneously once every 2 or 4 weeks per the treatment plan outlined by the physician. The nurse closely monitored and reported local injection site reactions and drug allergies within 2 hours of the injection. During omalizumab treatment, the treating physician followed the patient for an extended period, typically 3 years, per routine clinical practice. Every 4–6 months, the treating physician documented exacerbations (including hospitalisation), ICS/OCS exposure, and the use of an asthma controller (ie, LABA) or reliever (ie, short-acting beta-agonist). The symptoms and quality
of life of the patient were assessed every 4 weeks using the Asthma Control Test (ACT) and Mini-Asthma Quality of Life Questionnaire (Mini-AQLQ). Follow-up laboratory assessments were performed every 4–6 months or were clinically indicated. For study enrollment and data collection, the investigator screened clinic-treated patients based on initial medical history enquiries and laboratory assessments and collected data from routine clinical practice at weeks 16, 24, 52, 104 and 156 after omalizumab initiation. In addition, the investigator documented the treatment duration and reasons(s) for discontinuation. Patients had the right to withdraw their consent from the study, while omalizumab or other treatments were unaffected.

ACT and mini-AQLQ

The ACT is a five-item questionnaire (activity limitation, dyspnoea, sleep awakening, and use of rescue medication for the past 4 weeks). The minimum clinically significant difference is three points. The Mini-AQLQ (symptoms, activities, emotions and environment) demonstrates excellent reliability and requires only a few minutes to complete. A change in score greater than 0.5 is considered clinically significant.

Exposure and outcome measures

The treating physician determined the initial dosage of omalizumab per the baseline serum IgE level (cut-off, 300 IU/mL) and body weight, as suggested by the omalizumab prescribing information. For patients whose recommended dosage could not be found in the package insert (insufficient evidence to support dosing), the investigator assessed the asthma severity and symptom control based on clinical experience to determine the initial dose. The treatment duration (weeks) and treatment compliance were also documented.

The primary outcome was reduced exacerbation, measured as the proportion of patients who experienced exacerbation within 1 year of omalizumab initiation. Exacerbation was defined as worsening asthma symptoms requiring systemic corticosteroids, emergency visits or hospitalization. Secondary outcomes included OCS or ICS step-down, changes in ACT and Mini-AQLQ scores, forced expiratory volume in 1 s (FEV1), fractional exhaled nitrous oxide (FeNO) and blood eosinophils over time from baseline. The real-world effectiveness of omalizumab at each study time point was established if all the following criteria were met: (1) no exacerbation, (2) no add-on LABA/long-acting muscarinic antagonists, (3) ICS or OCS step-down over baseline, and (4) ACT score ≥16 or an increase ≥3.

Statistics analysis

Sample size consideration

The primary analysis was descriptive with a generalised linear model (GLM). The sample size calculation was based on the precision of exacerbation rates in routine clinical practice. The published studies suggested that the rate of clinically significant exacerbations in the first year of omalizumab treatment ranges from 40% to 60% among patients with moderate-to-severe asthma. To achieve two-sided precision (two-sided 95% CI) within 10% of a point estimate of 50% for the exacerbation rate, a sample size of 100 patients who completed the first-year follow-up was needed for the study. Considering a premature withdrawal of 20%–30% of patients from the study, a total sample size of at least 130 patients was sufficient to describe the exacerbation in real-world clinical settings.

Analysis population

The full analysis set (FAS) included patients (n=398) who received at least one dose of omalizumab and completed the visit at week 16. The clinically evaluable (CE) set included patients (n=225) who received omalizumab for at least 16 weeks and were followed for at least 1 year after omalizumab initiation. The CE set was used to analyse the primary outcome measures.

Analysis of endpoints

The proportion of patients who experienced exacerbation was presented as a point estimate with a corresponding 95% CI (normal approximation or Clopper-Pearson method). The exacerbation rates in the year before and after omalizumab initiation were compared using Bowker’s test for paired proportions in one group. A nominal logistic regression model (logit to the GLM) was constructed to include the exacerbation rate as the outcome and the study visit as the fixed-effect variable. The OR was estimated (Wald method) for exacerbation risk between study visits. For the number of exacerbations, a generalised linear mixed model (GLMM) was constructed to include the treatment duration and study visit as the fixed-effect variables and the actual omalizumab dosage scheme as the random-effect variable. The GLMM was fitted using the restricted maximum likelihood method, and the least squares mean with SEs and 95% CI were estimated. Statistical comparisons between the study visits (1 year before and after omalizumab and 2 years after omalizumab administration) were made using Dunnett’s test. Repeated-measures analysis of variance was performed to compare differences in ACT, FEV1, FeNO and eosinophil count between baseline and each study visit using a post hoc Tukey-Kramer HSD (honestly significant difference) test.

All statistical analyses were performed using SAS JMP V.16.2. GLM and GLMM were performed using SAS JMP V.17.1 (SAS Institute). A two-sided p<0.05 was considered statistically significant whenever applicable. This study did not include imputations for missing data.

Patient and public involvement

Omalizumab is a new and expensive drug for Chinese patients with moderate-to-severe asthma. Patients expected a robust effectiveness of this treatment and
judged whether it was worth the high costs. The investigators did not seek patient input for the study design and execution, although there was potential study participation. The results will be posted as educational materials for patient education programmes at the hospital’s asthma clinic.

RESULTS

Patient disposition and baseline characteristics

Of the 432 patients enrolled in the study, 398 (92.1%) were included in the FAS and 225 (52.1%) in the CE set. The investigator enrolled more patients than the planned sample size because of concerns about excessive premature withdrawals during the COVID-19 lockdown.

Table 1 summarises the baseline demographic and clinical characteristics of the FAS. Patients were subgrouped by treatment duration. Overall, the mean±SD age of patients was 48.8±14.1 years, and 45.5% (181/398) were male. The mean serum IgE levels were 487.9±688.6 IU/mL. The mean±SD disease duration of asthma was 7.5±8.1 years, with severe asthma accounting for 57.3%. Most patients (74.9%) were on baseline treatment with ICS combined with LABA. In all patients screened using allergy tests, the primary allergens were dust mites (33.8%), multiple sensitisations (25.1%), pollen (18.3%), mould (10.5%), pet fur (10.5%) and food (1.4%).

In the treatment subgroups, patients treated with omalizumab between 16 and 52 weeks had the lowest baseline serum IgE level (474.7 IU/mL). Patients treated with omalizumab for 52 weeks or more had a significantly higher rate of OCS+ICS/LABA use than those treated with omalizumab for 52 weeks or less (18.4% vs <5% in other subgroups).

Treatment pattern of omalizumab

The mean±SD treatment duration was 46.6±34.8 weeks (online supplemental table 1). Online supplemental figure 1 shows treatment patterns. The most frequently
used dosage regimen (31.4%) was 300 mg every 4 weeks. Of all patients, 14.4% received treatment for 4–16 weeks, 25.9% for 52–104 weeks and 5.5% for >104 weeks, respectively. The initial dose of omalizumab was considered adequate in 77.4% of all patients.

Table 2 summarises the data of 254 patients who discontinued omalizumab within the first year following treatment initiation. The investigator contacted all patients by phone or social media regarding reasons for discontinuation. Among those who discontinued treatment, 82.3% had good treatment compliance, 74.8% reported ‘asthma controlled and treatment discontinued’, and 14.8% reported ‘lack of efficacy’.

**Table 2** Treatment compliance in the first year following omalizumab initiation

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>4–16 weeks</th>
<th>16–52 weeks</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=37</td>
<td>N=217</td>
<td>N=254</td>
</tr>
<tr>
<td>Compliance</td>
<td>n % 95% CI</td>
<td>n % 95% CI</td>
<td>n % 95% CI</td>
</tr>
<tr>
<td>Good</td>
<td>17 46.0 29.5, 63.1</td>
<td>192 88.5 83.5, 92.4</td>
<td>209 82.3 77.8, 86.8</td>
</tr>
<tr>
<td>Insufficient*</td>
<td>20 54.1 36.9, 70.5</td>
<td>25 11.5 7.6, 16.5</td>
<td>45 17.7 13.2, 23.0</td>
</tr>
</tbody>
</table>

Reason for discontinuation

<table>
<thead>
<tr>
<th>Reason for discontinuation</th>
<th>n % 95% CI</th>
<th>n % 95% CI</th>
<th>n % 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma controlled and treatment discontinued</td>
<td>17 46.0 29.5, 63.1</td>
<td>173 79.7 73.8, 84.9</td>
<td>190 74.8 69.0, 80.0</td>
</tr>
<tr>
<td>COVID-19 lockdown</td>
<td>0 0.0 0.0, 9.5</td>
<td>10 4.6 2.2, 8.3</td>
<td>10 3.9 1.9, 7.1</td>
</tr>
<tr>
<td>Economic reason†</td>
<td>6 16.2 6.2, 32.0</td>
<td>2 0.9 0.1, 3.3</td>
<td>8 3.2 1.4, 6.1</td>
</tr>
<tr>
<td>Lack of efficacy</td>
<td>14 37.8 22.5, 55.2</td>
<td>29 13.4 9.1, 18.6</td>
<td>43 16.9 12.5, 22.1</td>
</tr>
<tr>
<td>Treatment intolerance</td>
<td>0 0.0 0.0, 9.5</td>
<td>3 1.4 0.3, 4.0</td>
<td>3 1.2 0.2, 3.4</td>
</tr>
</tbody>
</table>

95% CI was calculated based on normal approximation or Clopper-Pearson exact method whenever appropriate.

*Patients who did not receive any injection for 4 weeks or above during omalizumab treatment.

†The drug was too expensive to afford.

**Primary outcome**

Table 3 summarises the primary outcome analysis of the CE set. The proportion of patients who had exacerbations in the year before (80.4% (181/225, 95% CI 75.3% to 85.6%)) was higher than 1 year after omalizumab initiation (18.7% (42/225, 95% CI 13.6% to 23.8%)). A paired proportion comparison within one group using Bowker’s test suggested a before-and-after difference of −61.8% (95% CI −68.5 to −54.0, p<0.01) (online supplemental tables 2 and 3) show 2×2 contingency tables for before-and-after treatment for one group). The GLM estimated OR was 0.06 (95% CI 0.03 to 0.09, p<0.01). Omalizumab treatment significantly reduced the exacerbations in patients with moderate-to-severe asthma within 1 year of treatment initiation. In addition, the exacerbation rates did not differ significantly between patients treated for 16–52 weeks and those treated for >52 weeks. Among patients followed for 2 years, the exacerbation rate was 41.7% (30/72, 95% CI 30.3% to 53.1%). The proportion of patients hospitalised for exacerbations showed a similar trend.

**Figure 1** presents the GLMM analysis of the number of exacerbations (the before-and-after differences by the paired t-test are shown in online supplemental table 4). The differences in the mean number of exacerbations and hospitalisations based on exacerbations in the year before and after omalizumab initiation were −1.72 (95% CI −2.12 to −1.31, p<0.001) and −0.22 (95% CI −0.33 to −0.10, p=0.001), respectively.

**Secondary analysis**

**ACT and mini-AQLQ**

The ACT scores at different visits increased significantly compared with those at baseline (online supplemental figure 2). At week 52, the increase in ACT scores from baseline was 4.6 among patients who completed the questionnaires (n=143) (p<0.001). At week 156, an increase in ACT scores from a baseline of 3.2 was observed. The changes in the Mini-AQLQ scores were similar to those in ACT scores (online supplemental figure 3).

**Pulmonary function, circulating FeNO and eosinophil counts**

FEV1 actual/predicted (FEV1% predicted) and FEV1/FVC (FEV1%) were assessed (online supplemental figure 4). FEV1% significantly improved at week 24 from baseline (p<0.05) and remained between 67.1% and 72.1% throughout the study. FEV1% predicted showed a similar trend and was significantly higher at week 52 than baseline (p=0.001).

Omalizumab treatment reduced the FeNO levels from baseline to week 52 (p<0.001 for paired comparisons between baseline and weeks 16 and 24; (online supplemental figure 5). At week 156, the mean FeNO level was 34.6 ppb, which was numerically lower than the baseline (p=not significant). In contrast, there were no significant
### Table 3 The primary outcome analysis (CE)

<table>
<thead>
<tr>
<th>Event/treatment</th>
<th>Time point (visit) of clinical assessment</th>
<th>1 year prior</th>
<th>1-year FU</th>
<th>Difference*†</th>
<th>2-year FU</th>
<th>Difference*†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N (%)</td>
<td>95% CI</td>
<td>n/N (%)</td>
<td>95% CI</td>
<td>% (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Exacerbation</td>
<td>Overall</td>
<td>181/225 (80.4)</td>
<td>75.3, 85.6</td>
<td>42/225 (18.7)</td>
<td>13.6, 23.8</td>
<td>–61.8 (–68.5, –54.0)</td>
</tr>
<tr>
<td></td>
<td>16–52 weeks</td>
<td>83/101 (82.2)</td>
<td>74.7, 89.6</td>
<td>19/101 (18.8)</td>
<td>11.2, 26.4</td>
<td>–63.4 (–72.8, –53.4)</td>
</tr>
<tr>
<td></td>
<td>52+ weeks</td>
<td>98/124 (79.0)</td>
<td>71.9, 86.2</td>
<td>23/124 (18.5)</td>
<td>11.7, 25.4</td>
<td>–60.5 (–69.4, –49.6)</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>Overall</td>
<td>31/225 (13.8)</td>
<td>11.6, 22.6</td>
<td>7/225 (3.1)</td>
<td>0.8, 5.4</td>
<td>–10.7 (–15.7, –5.4)</td>
</tr>
<tr>
<td></td>
<td>16–52 weeks</td>
<td>14/101 (13.9)</td>
<td>7.1, 20.6</td>
<td>4/101 (4.0)</td>
<td>0.2, 7.8</td>
<td>–9.9 (–17.7, –1.7)</td>
</tr>
<tr>
<td></td>
<td>52+ weeks</td>
<td>17/124 (13.7)</td>
<td>7.7, 19.8</td>
<td>3/124 (2.4)</td>
<td>0.0, 5.1</td>
<td>–11.3 (–17.9, –4.3)</td>
</tr>
</tbody>
</table>

Data are presented as n/N, %, and corresponding 95% CI for point estimates and between-group differences. n=number of patients who had exacerbations or hospitalisation due to exacerbation; N=number of patients who were CE.

All comparisons were statistically significant with ‡marginally statistically insignificant and §statistically non-significant; CE: the patient who had omalizumab for ≥4 months and was followed up for at least 1 year.

*Paired data for exacerbations or hospitalisations in the year before and after omalizumab initiation were compared using Bowker’s test.

†Generalised linear model was constructed using nominal logistic regression for the binary outcome, and the OR with corresponding 95% CI by the Wald method. The generalised linear model included the study visit, 1 year before omalizumab treatment and 1-year FU, 2-year FU after omalizumab initiation as the fixed-effect variable.

CE, clinically evaluable; FU, follow-up.
differences in eosinophil counts between baseline and any of the study visits.

Modification of corticosteroid use

Table 4 displays modifications to OCS and ICS during the study follow-up. Among patients in the CE set, 67.4% discontinued OCS use, 19.5% had reductions in ICS doses, and 75.0% had no changes in ICS doses. Among patients who were CE and followed for 2 years after treatment initiation, 78.6% discontinued OCS, 29.2% reduced their ICS dose and 56.9% did not change their ICS dose.

Sustained effectiveness of omalizumab

The off-treatment duration was analysed for patients with sustained omalizumab effectiveness at weeks 52 and 104 (online supplemental table 5). At week 52, 54.6% (83/152, 95% CI 46.3 to 62.7) of all patients with sustained effectiveness continued omalizumab treatment; 22.4% (34/152, 95% CI 16.0 to 29.8) had an

Table 4 Corticosteroid use during treatment and follow-up (CE)

<table>
<thead>
<tr>
<th>Dose change</th>
<th>1-year follow-up</th>
<th>2-year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OCS N=43</td>
<td>ICS N=200</td>
</tr>
<tr>
<td></td>
<td>n (%) 95% CI</td>
<td>n (%) 95% CI</td>
</tr>
<tr>
<td>Dose reduction</td>
<td>9 (20.9) 10.0, 36.0</td>
<td>39 (19.5) 14.2, 25.7</td>
</tr>
<tr>
<td>Dose increase</td>
<td>0 (0.0) –</td>
<td>10 (5.0) 2.4, 9.0</td>
</tr>
<tr>
<td>Dose unchanged</td>
<td>2 (4.7) 0.6, 15.8</td>
<td>150 (75.0) 68.4, 80.8</td>
</tr>
<tr>
<td>Discontinued</td>
<td>29 (67.4) 51.5, 80.9</td>
<td>0 (0.0) –</td>
</tr>
<tr>
<td>Initiated</td>
<td>3 (7.0) 1.5, 19.1</td>
<td>1 (0.5) 0.0, 2.8</td>
</tr>
</tbody>
</table>

Data are presented as n (%) and 95% CI; 95% CI was calculated based on Clopper-Pearson exact method or normal approximation whenever appropriate.

--, not calculated; CE, clinically evaluable; ICS, inhaled corticosteroids; OCS, oral corticosteroids.
off-treatment duration of ≤12 weeks. At week 104, 47.4% (18/38, 95% CI 31.0 to 64.2) of all patients with sustained effectiveness had an off-treatment duration between 24 and 52 weeks, while 21.1% (8/38, 95% CI 9.6 to 37.3) continued treatment.

Adverse experiences in clinical practice

The investigator documented drug-related adverse events (AEs) in which a causal relationship with omalizumab could not be ruled out. Among 434 patients who received at least one dose of omalizumab, 5.2% (22/434, 95% CI 3.3 to 7.8) had local injection site reactions, and 3.1% (13/434, 95% CI 1.6 to 5.2) reported fatigue (online supplemental table 6). Three patients discontinued omalizumab treatment due to drug-related AEs. Importantly, no drug-related serious AEs were observed during this study. One patient developed a left-sided kidney tumour during the second year of treatment. The investigator concluded that tumour occurrence was not related to omalizumab treatment.

DISCUSSION

Findings from this prospective observational study suggest that omalizumab treatment significantly reduces exacerbations among Chinese patients with moderate-to-severe allergic asthma. In addition, omalizumab treatment had a steroid-sparing effect and improved asthma control over a relatively long period. Finally, this study did not report new adverse experiences compared with RCTs.

In moderate-to-severe asthma, episodes of exacerbation are critical determinants of asthma control. The most important finding of our study is the remarkable reduction in clinically significant exacerbations after omalizumab treatment. Previous RCTs reported that omalizumab was associated with significantly lower exacerbation rates (26%–58%) compared with placebo with short-term treatment (24–28 weeks). Some observational studies compared exacerbation rates in the year before and after omalizumab treatment, suggesting reduced exacerbation rates of 50%–75%. Our findings are consistent with those of previous observational studies of reduced exacerbations.

No robust evidence specifies the optimal treatment duration for omalizumab and its off-treatment sustained effectiveness. Some studies have suggested that omalizumab has an off-treatment effect of 1 year after 3–5 years of treatment. A pooled analysis of RCTs and observational studies showed the possibility of long-term off-treatment IgE suppression among omalizumab-treated patients, with IgE decreased by 54% per year. In our study, among patients with sustained effectiveness at the end of 2 years, nearly half discontinued omalizumab for 24–52 weeks during this period. Although these real-world data challenge the extensive treatment duration of omalizumab in clinical practice, further evidence is required to confirm its rational use.

Treatment guidelines recommend OCS for patients with uncontrolled severe asthma. China’s guidelines recommend short-term OCS use (5–7 days) for moderate-to-severe asthmatic exacerbations. In the past, more than 50% of patients with uncontrolled severe asthma required the addition of OCS for symptoms. Nevertheless, maintenance of OCS is associated with cumulative adverse experiences, such as dyspeptic disorders and obesity, and increases in healthcare costs. In RCTs and observational studies, omalizumab exhibited a steroid-sparing effect. A global observational study reported slightly reduced maintenance OCS use after 1 year of omalizumab treatment. Another cohort study revealed that 72% of Taiwanese patients stopped using OCS after 1 year of treatment with omalizumab. Our study showed that most patients discontinued OCS at the end of 1 and 2 years after omalizumab initiation. A higher rate of OCS discontinuation was associated with reduced exacerbations over time. However, our results should be interpreted with caution because of the limited patient sample size for the 2-year follow-up. However, the dose reductions in ICS were not remarkable, and no patient discontinued ICS at the end of the 1-year follow-up.

Increases in ACT and Mini-AQLQ scores demonstrated improvements in asthma control over time. Our findings are consistent with those of previous studies reporting increased ACT scores over 4 years of omalizumab treatment and 5–6 points over time. Another finding was a 9.0% increase in FEV1% predicted at the end of 1 year after omalizumab initiation, supported by previous studies (7.7%–20% after 4–12 months of treatment). Exacerbations worsen airway inflammation and promote airway remodelling, leading to a decline in lung function and more severe exacerbations. Pulmonary function improvement by omalizumab treatment contributed to reduced exacerbations. In addition, FeNO decreased in parallel with pulmonary function improvement and reduced exacerbation, although the reduction in eosinophil counts was not significant. We did not plan to recruit patients with high eosinophil counts, which may partly explain the slight decrease in eosinophil count over time. Reduced eosinophil count and FeNO levels associated with omalizumab treatment have been reported previously. A reduction of 24% in FeNO after 1 year of treatment was also observed. Inflammatory biomarkers may predict the clinical response to omalizumab and warrant further investigation.

The assessment of treatment compliance and adverse experiences in clinical practice is complex and relies on patient self-reporting. Our study included a relatively large number of patients to observe treatment patterns and adverse experiences. Most patients received appropriate initial doses, but omalizumab was discontinued within 1 year of treatment. Patients reported asthma control as the main reason for treatment discontinuation. Another retrospective study in China suggested that most patients terminated omalizumab because of the drug price or lack
of efficacy. Our analysis revealed no new adverse experiences compared with previous studies. One patient was diagnosed with kidney cancer that was unrelated to treatment. A pooled analysis of RCTs suggested no association between malignancy and omalizumab treatment. 

Our study has several limitations. The lack of a control group prevents comparative effectiveness research on omalizumab with other treatment options. Repeated measures of exacerbations may be subject to regression towards the mean, which is a source of bias (reduced exacerbations might be observed by chance). The COVID-19 pandemic intervened in follow-up laboratory and pulmonary function assessments. For safety analysis, the sample size may not be representative of the detection of a new safety experience in a real-world setting. Currently, omalizumab is not eligible for governmental reimbursement. As a result, patients chose to discontinue treatment once they achieved asthma control (74.8%) or could not afford it anymore (3.2%), precluding a fair evaluation of the sustained response and off-treatment effects of omalizumab. Finally, our study was a single-centre study, and the results may not be generalisable to clinical practice in China, where adherence to treatment guidelines differs across hospitals.

CONCLUSION
In real-world clinical practice, omalizumab treatment remarkably reduced exacerbations in Chinese patients with moderate-to-severe allergic asthma. Omalizumab treatment was associated with clinically relevant improvements in asthma control and pulmonary function, spared ICS use and reduced OCS exposure. No unexpected AEs associated with omalizumab were observed, and further investigations are required to determine the optimal treatment duration.

Supplemental material
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