Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Omalizumab

Trial Indication(s)
Allergic Asthma

Protocol Number
CIGE025BCN01

Protocol Title
A retrospective multicenter study for assessment of the effectiveness and safety of omalizumab in children with allergic asthma in a real-world setting in China

Clinical Trial Phase
NA

Phase of Drug Development
NA

Study Start/End Dates
Study start date: 25/02/2021

Study Completion date: 28/06/2021

Reason for Termination

NA

Study Design/Methodology

This non-interventional, retrospective study aimed to assess the effectiveness and safety of omalizumab in children with allergic asthma in China, and described patient profiles and treatment patterns of omalizumab in real-world practice. This study was designed to use secondary data from medical charts of 25 hospitals. Medical records were reviewed to collect information such as demographics, clinical characteristics, treatment patterns, effectiveness, and AEs for retrospective analysis. Patients with allergic asthma aged 6–12 years treated with omalizumab from July 6, 2018 to September 30, 2020 were identified for medical chart extraction.

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

- To evaluate the effectiveness of omalizumab among children aged 6–12 years with allergic asthma in China.

Secondary objective(s)

- To evaluate safety of omalizumab among children with allergic asthma in China.
- To evaluate other effectiveness outcomes of omalizumab among children with allergic asthma
- in China.
- To describe the treatment pattern of omalizumab among children with allergic asthma in China.

Test Product (s), Dose(s), and Mode(s) of Administration

NA

Statistical Methods

This was an observational and exploratory study. The statistical analysis was mainly descriptive. Unless otherwise specified, statistical hypotheses and tests were not involved. If hypotheses testing was used, all statistical tests should be interpreted at a 2-sided significance level of 5% and all confidence intervals (CI) should be presented at a 2-sided confidence level of 95%, unless otherwise specified.

Full analysis set (FAS): All enrolled patients who had at least one omalizumab treatment during the identification period and had at least one follow-up visit after omalizumab therapy.

Per protocol set (PPS): The PPS was a subset of the FAS. All patients in the FAS who met the inclusion criteria and with no protocol violation.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Aged between 6-12 years
- Diagnosed with allergic asthma and could be treated using omalizumab. Comorbidities included allergic rhinitis, atopic dermatitis, nasal polyp, chronic urticaria, and food allergy.
- Received omalizumab during the identification period
- Had at least one documented follow-up data after omalizumab treatment
- Provided informed consent if required by ethics committee (EC) of hospital

Exclusion criteria

- Current participation in a clinical trial of any investigational treatment.

Participant Flow

The overall study size was designed to be 200 patients, and 200 patients were successfully recruited.

Baseline Characteristics

A total of 200 allergic asthma patients were enrolled in the FAS, among which 151 patients (75.5%) were male and 49 (24.5%) were female. The age (mean ± SD) of these patients was 8.2 ± 1.81 years. The duration of allergic asthma (mean ± SD) of the 200 patients was 3.52 ± 2.501 years. Among those, 33 patients (16.5%) had mild asthma, 136 (68.0%) had moderate asthma, and 24 (12.0%) had severe asthma; the severity of 7 (3.5%) was unknown. A total of 189 patients (94.5%) had at least one allergic comorbidity. The most common comorbidities were allergic rhinitis in 175 patients (87.5%), atopic dermatitis/eczema in 52 patients (26.0%), and food allergy in 25 patients (12.5%). Overall, 180 patients (90.0%) had serum total IgE values at baseline, with the mean ± SD IgE level being 886.789 ± 1193.0874 IU/ml; 0.6% (1/180), 85.0% (153/180), and 14.4% (26/180) of these patients had total IgE levels <30 IU/ml, between 30–1500 IU/ml, and >1500 IU/ml, respectively. Twenty patients had no baseline serum total IgE data. The initial omalizumab dose of 11 out of the 20 patients was determined according to the IgE level tested before baseline; IgE values from three patients were not collected because of a hospital system update; two patients only had qualitative detection of total IgE, and the omalizumab dose was determined according to the qualitative detection; three patients had IgE tests at another hospital, but the results were not collected; one patient's IgE data was not input into the EDC. A total of 112 patients (56.0%) had a specific IgE test, among which 104 (92.9%) had at least one positive result.

Primary and Secondary Outcome Result(s)

Effectiveness outcomes

Among 26 PPS patients, 23 responded to omalizumab after 4‑6 months of treatment. The response rate (95% confidence interval) was 88.5% (69.85%, 97.55%).

Other effectiveness outcomes

Proportion of patients who responded to omalizumab after 4–6 months of treatment: After 4–6 months of treatment, 117 patients had GETE evaluation. Out of these, 16.2% (19/117) of the patients were evaluated simultaneously with ongoing treatment; 83.8% (98/117) were evaluated retrospectively based on medical data. The evaluations were categorized as excellent, good, and moderate for 21.4% (25/117), 76.9% (90/117), and 1.7% (2/117) of patients, respectively. None was evaluated as unchanged or worsening.

Asthma exacerbation:

Among the 200 FAS patients, 191 (95.5%) patients had evaluation of moderate-to-severe asthma exacerbation at baseline, and the annual rate (mean ± SD) at baseline was 2.026 ± 5.7559 per patient year; 190 patients were evaluated after treatment with a rate (mean ± SD) of 0.065 ±

0.3572 per patient year (P < 0.0001). Severe asthma exacerbation was evaluated among 192 (96.0%) patients at baseline and the rate (mean ± SD) was 0.391 ± 1.6239 per patient year. After treatment, 191 patients were evaluated, and the annual rate (mean ± SD) of severe asthma exacerbation was 0.010 ± 0.1344 per patient year. Compared to baseline, it reduced by 0.383 ± 1.6239 (mean ± SD) per patient year.
The frequency (mean ± SD) of moderate-to-severe asthma exacerbation and severe asthma exacerbation at baseline were 2.0 ± 5.76 and 0.4 ± 1.62, respectively. Compared to baseline, they each reduced by 2.0 ± 5.67 and 0.4 ± 1.63, respectively.

Glucocorticoid treatment:
Among the FAS patients, 83 had ICS treatment records at baseline; daily dosage (mean ± SD) was 317.5 ± 544.29 μg, and after 16–24 weeks of treatment, 82 had ICS treatment records with the daily dosage being 22.0 ± 58.40 μg. Daily dosage decreased by 298.2 ± 554.92 μg (88.6% ± 29.50%) from baseline. One patient received OCS at baseline (dosage unknown), which was discontinued after 2 days.

Lung function:
After 4–6 months of treatment, all pulmonary function measurements were improved.

	Baseline	After 16-24week treatment
FEV1	1.540±0.4535 L	Increase 0.221±0.1432 L
FEV1% pred	89.730±18.1713 %	Increase 7.284±8.3004 %
FEV1/FVC	81.558±10.8330 %	Increase 4.879±5.5820 %
PEF	3.534±1.0514 L/S	Increase 0.508±0.5822 L/S
MMEF	1.525±0.6453 L/S	Increase 0.513±0.3674 L/S

Omalizumab treatment pattern:
Among the 200 FAS patients, 114 patients received the recommended dosage instructions during the identification period. Among those patients, approximately half (51.8%, 59/114) followed the recommended dosage as per the dosing table/ label for their first injection dose; however, for 35 patients (30.7%), the first injection dose was less than the recommended, while 19 patients (16.7%) had a higher dose than recommended, one patient’s actual dosage was unknown,. In the identification period, 36 patients should have received the treatment fortnightly, as per the label recommendation. In reality, however, the interval of administration (mean ± SD) was 30.8 ± 13.87 days for the

36 patients. Among these patients, three (8.3%) patients received the injection once every 2 weeks, two (5.6%) patients once every 4 weeks, four (11.1%) patients once every 5 weeks, and twenty-five (69.4%) patients irregularly. Two patients failed to calculate the administration frequency. For 78 patients who should have received treatment once every 4 weeks, as per the label recommendation in the identification period, the actual interval time (mean ± SD) was 34.5 ± 11.08 days. One (1.3%) patient received the injection once every 2 weeks, nineteen patients (24.4%) once every 4 weeks, three (3.8%) patients once every 5 weeks, one (1.3%) patient once every 6 weeks, and forty-six (59.0%) patients irregularly. Eight patients failed to calculate the actual frequency of administration. The average duration (mean ± SD) of omalizumab therapy of the 200 patients was 158.9 ± 131.20 days. Five percent (10/200) of the patients received omalizumab therapy for less than 4 weeks. The proportion of patients who received omalizumab for 4-16 weeks was the highest (45.0%, 90/200). Additionally, 18.5% (37/200) patients had 16-24 weeks of omalizumab treatment, and 22.0% (44/200) had 24-52 weeks of omalizumab treatment; 9.5% (19/200) of patients received omalizumab for ≥52 weeks; 43.5% (87/200) of patients discontinued omalizumab during the identification period. The main reason for discontinuation for most patients (81.6%) was asthma control improvement.

Safety Results

A total of 124 AEs were reported by 58 patients (29.0%), and the annual incidence (mean ± SD) was 0.834 ± 1.9419 per patient year. Among all AEs, 44 (22.0%) and 9 (4.5%) were mild and moderate AEs, respectively. No patient reported severe AEs, and five (2.5%) did not report the severity of AEs.

Other Relevant Findings

None

Conclusion

In a real-world clinical setting, omalizumab showed good effectiveness for the treatment of asthma in children aged 6–12 years, and could improve asthma control and quality of life, while reducing asthma exacerbations and ICS dosage. Safety features were similar to those of previous studies.

Date of Clinical Study Report

19 March 2021