Journal of Asthma and Allergy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Efficacy and Safety of Omalizumab Combined with Allergen-Specific Immunotherapy in the Treatment of Moderate-to-Severe Allergic Asthma: A Prospective Cohort Study in a Chinese Population

Na Liu[1,*], Peng Jin[2,*], Xu Li[1], Tingting Gao[1], Yan Sun[1], Na Zhang[1], Yunqing Zhang[1], Peize Liu[1,3], Hailing Zhang[2], Lili Zhi[1]

[1]Department of Allergy, Shandong Provincial Qianfoshan Hospital, Shandong Institute of Respiratory Diseases, The First Affiliated Hospital of Shandong First Medical University, Jinan, 250014, People's Republic of China; [2]Department of Otolaryngology, The Second Qilu Hospital of Shandong University, Jinan, 250033, People's Republic of China; [3]Shandong First Medical University, Shandong Academy of Medical Sciences, Jinan, 250117, People's Republic of China

*These authors contributed equally to this work

Correspondence: Lili Zhi Department of Allergy, Shandong Provincial Qianfoshan Hospital, Shandong Institute of Respiratory Diseases, The First Affiliated Hospital of Shandong First Medical University, No. 16766, Jingshi Road, Jinan, Shandong, 250014, People's Republic of China, Email qfsyyallergy@163.com; Hailing Zhang Department of Otolaryngology, The Second Qilu Hospital of Shandong University, 247 Beiyuan Avenue, Jinan, 250033, People's Republic of China, Email 15853138360@163.com

Background: Moderate-to-severe allergic asthma caused by dust mite sensitization is challenging to treat. Allergen-specific immunotherapy (AIT) is the only disease-modifying option but is limited by delayed effects, allergic side reactions, and poor adherence. Omalizumab, an anti-IgE antibody, may improve AIT's safety and effectiveness.

Objective: To assess whether combining omalizumab with AIT is more effective and safer than AIT alone in patients with dust mite-induced moderate-to-severe asthma.

Methods: This prospective study involved 37 patients divided into two groups: AIT alone (n=18) and omalizumab + AIT (n=19). Over 48 weeks, asthma control (ACT, ACQ), lung function (FEV_1%, PEF%, FEV_1/FVC), and airway inflammation (FeNO) were measured. Secondary outcomes included IgE levels, eosinophil counts, quality of life (AQLQ), and safety.

Results: Both groups improved, but the combination group showed significantly better asthma control, lung function, and quality of life at week 48. Only the combination group had significant reductions in FeNO and eosinophils, suggesting stronger anti-inflammatory effects. IgE levels followed expected trends with no major group differences. Fewer adverse reactions occurred in the combination group; severe systemic events were reported only in the AIT-alone group.

Conclusion: Adding omalizumab to AIT significantly enhances asthma control, lung function, and inflammation reduction while improving treatment safety. This supports its role as an effective adjunct in managing moderate-to-severe dust mite-allergic asthma in Chinese patients.

Keywords: asthma, allergen immunotherapy, omalizumab, allergy, efficacy, safety, treatment

Introduction

Bronchial asthma is a chronic inflammatory airway disease characterized by airway hyperresponsiveness, airway remodeling, and reversible airflow limitation. Its high prevalence imposes a significant economic and social burden worldwide, affecting millions of individuals across different age groups. Asthma is a complex and multifactorial condition influenced by genetic predisposition, environmental triggers, and immune dysregulation.[1,2] With advancements in phenotypic research and mechanistic discoveries, it is now recognized as a heterogeneous disease with distinct clinical phenotypes and underlying molecular mechanisms. Among these, allergic asthma is the most common and clinically

Received: 16 April 2025
Accepted: 30 August 2025
Published: 23 September 2025

significant phenotype, accounting for more than half of adult asthma cases and up to 80% of childhood asthma cases.[3–5] The strong link between allergic sensitization and asthma severity underscores the critical role of allergen-specific immune responses in disease progression, particularly in patients with persistent exposure to environmental allergens. In China, house dust mites are the predominant allergen contributing to allergic asthma, making dust mite-induced asthma a major public health concern.[6–8]

Allergen-specific immunotherapy is the only disease-modifying treatment available for allergic asthma, offering long-term benefits by desensitizing the immune system to allergens.[9,10] However, its clinical application is often hampered by the need for prolonged treatment duration, variable response rates, and the risk of systemic allergic reactions. These limitations frequently lead to treatment discontinuation and poor adherence, reducing its effectiveness in real-world settings.[11,12] On the other hand, biologic therapies have transformed the management of moderate-to-severe asthma by specifically targeting key inflammatory pathways.[13,14] Among them, omalizumab, an anti-IgE monoclonal antibody, has been shown to significantly improve asthma control, reduce exacerbations, and lower corticosteroid dependence, particularly in patients with high IgE levels and multiple allergic sensitizations.[15,16] By blocking IgE from binding to effector cells such as mast cells and basophils, omalizumab reduces allergic inflammation and airway hyperresponsiveness, leading to better disease control.[17,18]

Both AIT and omalizumab have demonstrated clinical benefits, but whether their combination offers superior outcomes remains an area of interest.[19–22] Theoretically, omalizumab could enhance the safety and effectiveness of AIT by mitigating early-phase allergic reactions and facilitating better tolerance to immunotherapy, potentially leading to improved adherence and long-term efficacy. Previous studies have suggested that the combination of omalizumab with AIT may provide a more comprehensive approach to asthma management by addressing both immediate allergic responses and long-term immune modulation.[23,24] However, despite its potential advantages, clinical data on the combined use of omalizumab and AIT remain limited, particularly in Chinese populations with dust mite-induced asthma. Given the high burden of allergic asthma in this population, further research is needed to evaluate whether this combination therapy can offer significant clinical benefits. This study aims to investigate the efficacy and safety of combining omalizumab with AIT in patients with moderate-to-severe allergic asthma sensitized to dust mites. By analyzing clinical outcomes over a 48-week follow-up period, this study seeks to determine whether the addition of omalizumab to AIT improves asthma control, reduces corticosteroid dependence, and enhances patient adherence compared to AIT alone. Understanding the potential benefits of this combination therapy could provide new insights into optimizing asthma management strategies and improving treatment outcomes for patients with allergic asthma.

Materials and Methods

Study Design

This study complies with the Declaration of Helsinki. This was a prospective cohort study conducted at The First Affiliated Hospital of Shandong First Medical University, Shandong Provincial Qianfoshan Hospital, designed to evaluate the efficacy and safety of combining omalizumab (Omalizumab alfa for Injection, Taizhou Mabtech Pharmaceutical Co. Ltd., China) with allergen-specific immunotherapy (Alutard SQ®, ALK) in patients with moderate-to-severe allergic asthma sensitized to house dust mites. Patients were enrolled and assigned to one of two groups: an AIT-alone group receiving subcutaneous allergen-specific immunotherapy (SCIT) targeting dust mites following a standard dose-escalation protocol, and an Omalizumab + AIT group, in which patients received omalizumab concurrently with SCIT from the initiation of treatment. The study followed patients for 48 weeks, with clinical and laboratory assessments conducted at baseline, 12, 24, and 48 weeks.

Participants

Eligible participants were aged 18 to 65 with a diagnosis of moderate-to-severe allergic asthma, as defined by the Global Initiative for Asthma (GINA) guidelines. Sensitization to house dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae) was confirmed via serum-specific IgE testing and skin prick test (SPT). Patients were required to have poor asthma control despite regular inhaled corticosteroids (ICS) and long-acting beta-agonists

(LABA) therapy. Exclusion criteria included severe uncontrolled asthma requiring frequent oral corticosteroids or hospitalization, other respiratory diseases such as chronic obstructive pulmonary disease (COPD) or bronchiectasis, history of anaphylaxis to AIT, contraindications to omalizumab, active smoking, pregnancy, or lactation.

Treatment Protocol and Outcome Measures

Patients in the AIT group received SCIT following a dose-escalation schedule with weekly injections during the build-up phase and maintenance injections administered every 4 to 6 weeks. In the Omalizumab + AIT group, patients received omalizumab at doses ranging from 150 to 600 mg every 2 to 4 weeks, based on baseline IgE levels and body weight, following manufacturer recommendations. Omalizumab was initiated simultaneously with AIT to assess whether it could enhance the safety and efficacy of immunotherapy from the beginning of treatment. Primary outcomes included improvement in asthma control, assessed by the Asthma Control Test (ACT) and Asthma Control Questionnaire (ACQ), and changes in pulmonary function parameters, including forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), and fractional exhaled nitric oxide (FeNO). Secondary outcomes included changes in total IgE and specific IgE to dust mites, peripheral eosinophil counts as a marker of inflammation, and quality of life assessed using the Asthma Quality of Life Questionnaire (AQLQ). Adverse reactions to treatment, including local and systemic allergic reactions, were recorded.

Follow-up Assessments

Patients were evaluated at baseline, 12, 24, and 48 weeks. Each visit included clinical assessments of asthma control scores (ACT, ACQ), pulmonary function testing (FEV_1, PEF, FeNO), and biomarker evaluation (total IgE, specific IgE, eosinophil counts). Adverse reactions related to AIT and omalizumab were recorded at each visit.

Adverse Event Monitoring

All adverse reactions were documented, including local injection site reactions and systemic allergic responses. Local reactions, such as erythema and swelling, were classified by severity, while systemic reactions, including urticaria, angioedema, bronchospasm, and anaphylaxis, were recorded using standard classification criteria. Severe systemic reactions resulted in discontinuation of AIT, with reassessment of omalizumab continuation. All adverse reactions were classified based on severity into mild, moderate, and severe reactions. Mild systemic reactions included urticaria that was self-limiting, transient wheezing responsive to bronchodilator use, mild dyspnea without significant airway obstruction, and gastrointestinal discomfort such as nausea or vomiting that resolved spontaneously. Moderate systemic reactions included generalized urticaria requiring antihistamines, persistent wheezing or dyspnea requiring bronchodilators or corticosteroids, and gastrointestinal symptoms requiring intravenous fluids or antiemetics. Severe systemic reactions included bronchospasm with marked airway narrowing requiring emergency bronchodilators, angioedema with swelling of the lips, face, or throat posing a risk of airway obstruction, hypotension indicative of anaphylaxis requiring intravenous fluids or epinephrine, and anaphylactic shock requiring emergency resuscitation. All patients were monitored for at least 30 minutes post-injection to document immediate allergic reactions, while delayed reactions occurring within 24–48 hours were reported through structured questionnaires or phone follow-ups. Reactions were recorded with details including time of onset, duration, required interventions, and resolution status.

Statistical Analysis

Data were analyzed using SPSS and R software. Normality was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using Student's t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical data. Repeated measures analysis of variance (ANOVA) was used to analyze changes over time. A p-value < 0.05 was considered statistically significant. The Benjamini-Hochberg procedure was applied to correct for multiple comparisons.

Results

Baseline Characteristics

A total of 37 patients were enrolled, with 18 assigned to the AIT group and 19 to the Omalizumab + AIT group. Baseline demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences in age, gender distribution, BMI, smoking history, or asthma severity. The mean age was 45.3 ± 8.4 years in the AIT group and 44.1 ± 9.3 years in the Omalizumab + AIT group ($p = 0.73$). (Table 1).

Asthma Control and Quality of Life Improvements

Both groups showed improvements in asthma control over time, but the Omalizumab + AIT group demonstrated significantly greater improvements at each follow-up. At 48 weeks, ACT scores increased from 16.8 ± 4.3 to 18.9 ± 2.9 in the AIT group and from 17.2 ± 4.5 to 21.8 ± 2.7 in the Omalizumab + AIT group ($p < 0.01$). Similarly, ACQ scores improved from 2.6 ± 1.2 to 1.9 ± 0.8 in the AIT group and from 2.8 ± 1.3 to 1.2 ± 0.7 in the Omalizumab + AIT group ($p < 0.01$). The AQLQ scores indicated significant quality-of-life improvements in both groups, with the Omalizumab + AIT group experiencing a greater magnitude of improvement (Table 2) (Figure 1).

Inflammatory Biomarkers and IgE Changes

Total IgE levels exhibited an expected increase in the AIT group, rising from 185.5 ± 45.0 kU/L to 200.4 ± 37.5 kU/L, whereas the Omalizumab + AIT group showed a decrease from 192.3 ± 48.2 kU/L to 178.2 ± 36.4 kU/L ($p = 0.07$). Specific IgE to dust mites followed a similar trend, with a slight increase in both groups, showing no significant difference at 48 weeks ($p = 0.14$). Peripheral eosinophil counts remained stable in the AIT group ($p = 0.11$) but showed a significant reduction in the Omalizumab + AIT group ($p < 0.001$), suggesting an anti-inflammatory effect of omalizumab. FeNO levels decreased significantly in the Omalizumab + AIT group compared to the AIT group at 48 weeks ($p < 0.01$), indicating reduced airway inflammation (Table 3) (Figure 1).

Table 1 Baseline Demographic and Clinical Characteristics

Variable	AIT Group (n=18)	Omalizumab + AIT Group (n=19)	p-value
Age (Mean ± SD)	45.3 ± 8.4	44.1 ± 9.3	0.73
Gender (Male/Female)	10 / 8	11 / 8	0.81
BMI (Mean ± SD)	24.6 ± 3.1	25.2 ± 2.9	0.58
Normal Weight (BMI < 24.9)	10 (55.6%)	9 (47.4%)	0.69
Overweight (BMI 25–29.9)	6 (33.3%)	7 (36.8%)	0.81
Obese (BMI ≥ 30)	2 (11.1%)	3 (15.8%)	0.82
Never Smoked	14 (77.8%)	15 (78.9%)	0.94
Former Smoker	3 (16.7%)	3 (15.8%)	0.96
Current Smoker	1 (5.6%)	1 (5.3%)	1.00
Family History of Asthma	7 (38.9%)	8 (42.1%)	0.84
Comorbid Allergies	4 (22.2%)	5 (26.3%)	0.74
Previous Use of Biologics	3 (16.7%)	2 (10.5%)	0.74

Notes: The table summarizes the baseline demographic and clinical characteristics of patients in the AIT group (n = 18) and the Omalizumab + AIT group (n = 19) before the initiation of treatment.

Table 2 48-Week Follow-up on Clinical Outcomes

Clinical Data	Time Point	AIT Group (Mean ± SD)	Omalizumab + AIT Group (Mean ± SD)	P-value	p-value (Baseline vs 48 Weeks)
Asthma Control Test (ACT)	Baseline	16.8 ± 4.3	17.2 ± 4.5	0.75	
	12 Weeks	16.5 ± 4.1	18.7 ± 3.8	0.1	
	24 Weeks	17.5 ± 3.7	20.5 ± 3.4	*0.02	
	48 Weeks	18.9 ± 2.9	21.8 ± 2.7	*<0.01	AIT: 0.08, Omalizumab + AIT: <0.01*
Asthma Control Questionnaire (ACQ)	Baseline	2.6 ± 1.2	2.8 ± 1.3	0.81	
	12 Weeks	2.7 ± 1.1	1.9 ± 1.0	*0.03	
	24 Weeks	2.3 ± 0.9	1.5 ± 0.9	*0.02	
	48 Weeks	1.9 ± 0.8	1.2 ± 0.7	*0.01	AIT: 0.06, Omalizumab + AIT: <0.01*
Quality of Life Score (AQLQ Score)	Baseline	4.4 ± 1.2	4.3 ± 1.1	0.92	
	12 Weeks	4.7 ± 1.1	5.3 ± 1.0	*0.03	
	24 Weeks	5.1 ± 1.2	6.0 ± 1.1	*0.02	
	48 Weeks	5.7 ± 1.0	6.5 ± 1.0	*<0.05	AIT: 0.08, Omalizumab + AIT: <0.01*

Notes: The changes in clinical outcome measures over a 48-week follow-up period in patients receiving allergen-specific immunotherapy (AIT) alone versus those receiving omalizumab in combination with AIT. *Values marked with an asterisk indicate statistical significance ($p < 0.05$).

Pulmonary Function Changes

Pulmonary function tests revealed that FEV_1% predicted increased from 79.5 ± 4.0% to 84.5 ± 3.0% in the AIT group and from 81.0 ± 4.0% to 91.5 ± 3.0% in the Omalizumab + AIT group ($p < 0.01$). PEF% predicted improved from 74.8 ± 4.8% to 80.2 ± 3.8% in the AIT group and from 76.5 ± 4.8% to 87.0 ± 3.8% in the Omalizumab + AIT group ($p < 0.01$). The FEV_1/FVC ratio (%) improved in both groups but was more pronounced in the Omalizumab + AIT group ($p = 0.02$ at 48 weeks) (Table 4) (Figure 1).

Adverse Reactions and Safety Outcomes

Adverse reactions were more frequent in the AIT group compared to the Omalizumab + AIT group, particularly at later follow-ups. Local injection site reactions occurred in 33.3% of AIT patients at 48 weeks compared to 21.1% in the Omalizumab + AIT group ($p = 0.21$). Mild systemic reactions were observed in 11.1% of AIT patients and 5.3% of Omalizumab + AIT patients ($p = 0.32$). Importantly, severe systemic reactions (bronchospasm) occurred in 5.6% of AIT patients at each follow-up visit but were not observed in the Omalizumab + AIT group ($p = 0.49$)No cases of anaphylaxis were recorded in either group. These findings suggest that the addition of omalizumab to AIT improves the safety profile of immunotherapy by reducing systemic allergic reactions, thereby potentially enhancing patient adherence (Table 5).

Discussion

Our study demonstrated that the combination of omalizumab with AIT provides greater clinical benefits compared to AIT alone in patients with moderate-to-severe allergic asthma sensitized to house dust mites. Over the 48-week follow-up period, patients receiving omalizumab in combination with AIT exhibited significantly improved asthma control, enhanced pulmonary function, and better quality of life compared to those receiving AIT alone. Additionally, the combination therapy was associated with a lower incidence of systemic allergic reactions, particularly severe systemic reactions, reinforcing its potential role in improving the safety profile of AIT. The improvement in asthma control was evident in both treatment

https://doi.org/10.2147/JAA.S530738

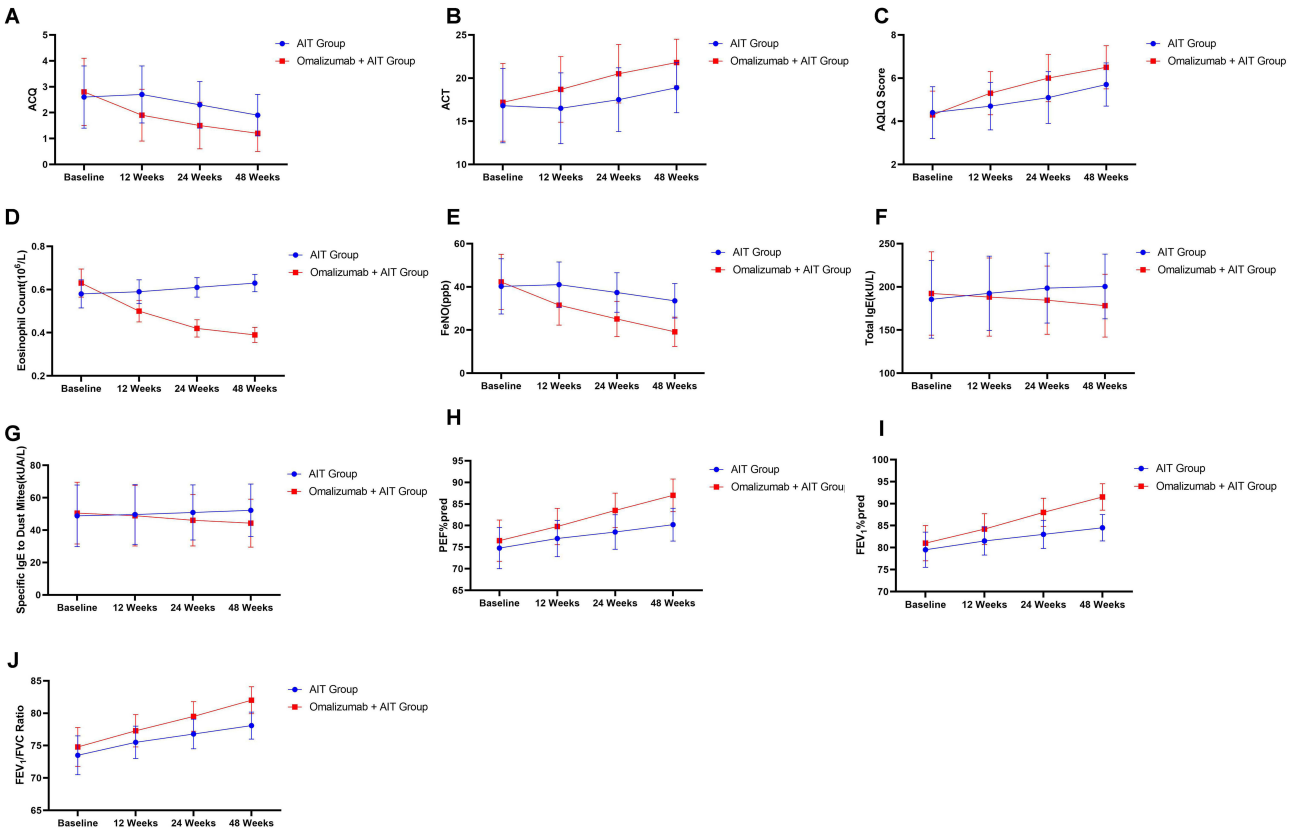

Figure 1 Clinical, laboratory, and pulmonary parameters over a 48-week follow-up period in the AIT group and the Omalizumab + AIT group. (**A**) Asthma Control Questionnaire (ACQ) scores decreased over time in both groups, with greater reductions in the combination group. (**B**) Asthma Control Test (ACT) scores increased progressively, with higher improvements observed in the Omalizumab + AIT group. (**C**) Asthma-related quality of life (AQLQ) scores improved in both groups, significantly favoring the combination therapy. (**D**) Peripheral blood eosinophil counts decreased significantly in the Omalizumab + AIT group but remained stable in the AIT group. (**E**) Fractional exhaled nitric oxide (FeNO) levels declined in both groups, with a more marked reduction in the combination group. (**F**) Total IgE levels slightly increased in the AIT group and showed a modest decline in the Omalizumab + AIT group. (**G**) Specific IgE to dust mites showed minimal changes and no significant between-group differences. (**H**) Peak expiratory flow (PEF)% predicted improvement in both groups, with a steeper increase in the Omalizumab + AIT group. (**I**) FEV_1% predicted improvement over time in both groups, with a statistically greater improvement in the combination group. (**J**) FEV_1/FVC ratio (%) increased progressively in both groups, again with more pronounced changes in the Omalizumab + AIT group.

groups; however, patients in the omalizumab + AIT group achieved superior outcomes, as reflected in higher ACT scores and lower ACQ scores at all follow-up visits. This suggests that omalizumab enhances the efficacy of AIT by reducing airway inflammation and stabilizing allergic responses, leading to better symptom management. These findings align with previous studies indicating that omalizumab improves asthma control in patients with high IgE levels and multiple allergic sensitizations. Moreover, pulmonary function measures, including FEV_1% predicted, PEF% predicted, and FEV_1/FVC

Table 3 48-Week Follow-up on Laboratory Markers

Laboratory Data	Time Point	AIT Group (Mean ± SD)	Omalizumab + AIT Group (Mean ± SD)	p-value	p-value (Baseline vs 48 Weeks)
Total IgE (kU/L)	Baseline	185.5 ± 45.0	192.3 ± 48.2	0.87	
	12 Weeks	192.5 ± 43.0	188.2 ± 45.3	0.8	
	24 Weeks	198.6 ± 40.5	184.6 ± 39.5	0.43	
	48 Weeks	200.4 ± 37.5	178.2 ± 36.4	0.08	AIT: 0.18 Omalizumab + AIT: 0.07

(*Continued*)

Table 3 (Continued).

Laboratory Data	Time Point	AIT Group (Mean ± SD)	Omalizumab + AIT Group (Mean ± SD)	p-value	p-value (Baseline vs 48 Weeks)
Specific IgE to Dust Mites (kUA/L)	Baseline	48.8 ± 19.0	50.5 ± 19.1	0.9	
	12 Weeks	49.6 ± 18.5	48.9 ± 18.7	0.88	
	24 Weeks	50.9 ± 17.0	46.1 ± 15.9	0.75	
	48 Weeks	52.2 ± 16.2	44.3 ± 14.8	0.13	AIT: 0.31 Omalizumab + AIT: 0.14
Eosinophil Count (10^9/L)	Baseline	0.58 ± 0.065	0.63 ± 0.065	0.79	
	12 Weeks	0.59 ± 0.055	0.50 ± 0.050	*0.05	
	24 Weeks	0.61 ± 0.045	0.42 ± 0.040	*<0.001	
	48 Weeks	0.63 ± 0.040	0.39 ± 0.035	*<0.001	AIT: 0.11, Omalizumab + AIT:<0.001*
FeNO (ppb)	Baseline	40.2 ± 12.8	42.3 ± 12.8	0.62	
	12 Weeks	41.0 ± 10.5	31.5 ± 9.3	*<0.01	
	24 Weeks	37.4 ± 9.2	25.1 ± 8.2	*<0.001	
	48 Weeks	33.5 ± 8.0	19.2 ± 6.8	*<0.001	AIT: 0.12, Omalizumab + AIT: <0.01*

Notes: The longitudinal changes in total IgE, specific IgE to dust mites, peripheral blood eosinophil counts, and fractional exhaled nitric oxide (FeNO) over 48 weeks in the AIT and Omalizumab + AIT groups. *Values marked with an asterisk indicate statistical significance ($p < 0.05$).

Table 4 48-Week Follow-up on Pulmonary Function Parameter

Pulmonary Function Parameter	Time Point	AIT Group (Mean ± SD)	Omalizumab + AIT Group (Mean ± SD)	p-value	p-value (Baseline vs 48 Weeks)
FEV_1% Predicted	Baseline	79.5 ± 4.0	81.0 ± 4.0	0.26	
	12 Weeks	81.5 ± 3.5	84.2 ± 3.5	0.06	
	24 Weeks	83.0 ± 3.2	88.0 ± 3.2	*0.03	
	48 Weeks	84.5 ± 3.0	91.5 ± 3.0	<0.001	AIT: 0.12 Omalizumab + AIT: <0.01*
PEF% Predicted	Baseline	74.8 ± 4.8	76.5 ± 4.8	0.29	
	12 Weeks	77.0 ± 4.2	79.8 ± 4.2	*0.05	
	24 Weeks	78.5 ± 4.0	83.5 ± 4.0	*0.02	
	48 Weeks	80.2 ± 3.8	87.0 ± 3.8	<0.001	AIT: 0.15 Omalizumab + AIT: <0.01*
FEV_1/FVC Ratio (%)	Baseline	73.5 ± 3.0	74.8 ± 3.0	0.2	
	12 Weeks	75.5 ± 2.5	77.3 ± 2.5	0.07	
	24 Weeks	76.8 ± 2.3	79.5 ± 2.3	*<0.001	
	48 Weeks	78.1 ± 2.1	82.0 ± 2.1	*<0.001	AIT: 0.18 Omalizumab + AIT: 0.02*

Notes: The longitudinal changes in pulmonary function parameters in the AIT group (n = 18) and the Omalizumab + AIT group (n = 19) over a 48-week follow-up period. The p-value column represents the between-group comparisons at each time point, while the p-value (Baseline vs 48 Weeks) column reflects the statistical significance of within-group changes. *Values marked with an asterisk indicate statistical significance ($p < 0.05$).

Table 5 Adverse Reactions Across Follow-up Visits

Time Point	Reaction Type	AIT Group (n=18)	Omalizumab + AIT Group (n=19)	p-value
12 Weeks	Local Injection Site Reactions	3 (16.7%)	2 (10.5%)	0.28
	Mild Systemic Reactions	2 (11.1%)	1 (5.3%)	0.41
	Severe Systemic Reactions	1 (5.6%)	0 (0.0%)	0.49
24 Weeks	Local Injection Site Reactions	4 (22.2%)	3 (15.8%)	0.22
	Mild Systemic Reactions	2 (11.1%)	1 (5.3%)	0.39
	Severe Systemic Reactions	1 (5.6%)	0 (0.0%)	0.49
48 Weeks	Local Injection Site Reactions	6 (33.3%)	4 (21.1%)	0.21
	Mild Systemic Reactions	2 (11.1%)	1 (5.3%)	0.32
	Severe Systemic Reactions	1 (5.6%)	0 (0.0%)	0.49

Notes: The table presents the incidence of adverse reactions in the AIT group (n=18) and the Omalizumab + AIT group (n=19) at 12, 24, and 48 weeks, categorized as local injection site reactions, mild systemic reactions, and severe systemic reactions.

ratio, showed significantly greater improvements in the combination therapy group, further supporting the hypothesis that omalizumab may mitigate airway remodeling and hyperresponsiveness when used alongside AIT.

The analysis of inflammatory biomarkers revealed notable differences between the two treatment groups. As expected, total IgE and specific IgE to dust mites increased in the AIT group, following the typical immunologic response to allergen exposure during immunotherapy. In contrast, total IgE levels in the omalizumab + AIT group showed a slight decrease over time, likely due to omalizumab's ability to neutralize free IgE and prevent its interaction with mast cells and basophils. Specific IgE levels did not differ significantly between the two groups, consistent with the understanding that AIT leads to the generation of blocking antibodies rather than a direct reduction in allergen-specific IgE. However, eosinophil counts exhibited a significant reduction in the omalizumab + AIT group but remained stable in the AIT-alone group, suggesting that omalizumab exerts additional anti-inflammatory effects beyond IgE blockade, contributing to a more favorable immunologic response. The safety analysis further supports the advantage of combining omalizumab with AIT. Local injection site reactions were common in both groups, though slightly less frequent in the combination therapy group. Mild systemic reactions were reported in both groups but were numerically lower in the omalizumab + AIT group. Importantly, severe systemic reactions, including bronchospasm, were observed only in the AIT-alone group, although the difference was not statistically significant. The absence of severe systemic reactions in the omalizumab + AIT group suggests that omalizumab may attenuate the early-phase allergic reactions associated with AIT, reducing the risk of systemic hypersensitivity responses. These findings align with previous reports suggesting that omalizumab may improve the tolerability of AIT, potentially increasing treatment adherence and long-term effectiveness. Mechanistically, omalizumab works by binding to free serum IgE, reducing its availability to bind high-affinity IgE receptors (FcεRI) on the surface of mast cells and basophils. This not only prevents allergen-induced activation of these effector cells but also leads to gradual downregulation of FcεRI expression, thereby dampening the potential for allergic responses over time. In the context of AIT, where controlled exposure to allergens can initially provoke IgE-mediated symptoms, the addition of omalizumab appears to stabilize the immune response and reduce early-phase reactions. This more tolerable immune environment may allow AIT to proceed with fewer interruptions or adverse events.[25,26]

Despite these promising findings, our study has several limitations that should be considered and addressed in the future. First, the sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of our results. Secondly, the follow-up period of 48 weeks, while sufficient to evaluate early treatment responses, may not capture the long-term effects of omalizumab on AIT outcomes. Third, the study was not blinded, which may introduce measurement bias, particularly for subjective outcomes such as ACT scores. Fourth, the use of patient-reported questionnaires

introduces a degree of subjectivity, which, although supported by objective clinical markers, may still influence outcome interpretation. Fifth, while we evaluated clinical efficacy and immunologic biomarkers such as IgE and eosinophil counts, we did not assess long-term immunomodulatory effects or memory immune responses, which would be valuable in understanding the sustained impact of combination therapy. Another limitation of our study is the absence of an omalizumab-only treatment arm. Although our findings suggest that combining omalizumab with AIT yields superior outcomes compared to AIT alone, previous randomized trials and meta-analyses consistently compared omalizumab plus AIT against AIT alone, without including an omalizumab-only control group.[20] Importantly, the mechanisms of omalizumab and AIT are distinct and complementary; omalizumab acts by neutralizing circulating IgE and reducing effector cell activation, whereas AIT induces long-term immune tolerance through regulatory T and B cell responses, suggesting that their therapeutic effects are not mutually exclusive. Future studies with larger patient cohorts and longer follow-up durations are needed to validate these findings and further explore the mechanistic interactions between omalizumab and AIT in modulating allergic inflammation. In conclusion, our study provides evidence that the combination of omalizumab with AIT offers superior efficacy and safety compared to AIT alone in patients with moderate-to-severe allergic asthma sensitized to house dust mites. The combination therapy leads to greater improvements in asthma control, lung function, and inflammatory biomarkers while reducing the risk of systemic allergic reactions. These findings suggest that omalizumab may serve as a valuable adjunct to AIT, enhancing its clinical benefits and safety profile and thereby providing a more effective approach for personalized asthma management.

Conclusion

Our study suggests that combining omalizumab with AIT offers clinical benefits for patients with moderate-to-severe allergic asthma sensitized to house dust mites. The combination therapy resulted in better asthma control, improved lung function, and reduced airway inflammation compared to AIT alone. These findings indicate that omalizumab may be a valuable addition to AIT, potentially improving treatment adherence and long-term outcomes. However, further studies with larger sample sizes and longer follow-up periods are needed to confirm these results and explore the long-term effects of this combination therapy in asthma management.

IRB Approval Status

This study was approved by the Institutional Review Board (IRB) of The First Affiliated Hospital of Shandong First Medical University, Shandong Provincial Qianfoshan Hospital, Approval number, YXLL-KY-2024 (061).

Informed Consent Statement

The written informed consent was obtained from all participants involved in this study.

Funding

This study was supported by the Shandong Provincial Natural Science Foundation (ZR2022MH283).

Disclosure

Na Liu and Peng Jin are co-first authors for this study. The authors declare that they have no relevant conflicts of interest in this work.

References

1. Miller RL, Grayson MH, Strothman K. Advances in asthma: new understandings of asthma's natural history, risk factors, underlying mechanisms, and clinical management. *J Allergy Clin Immunol*. 2021;148(6):1430–1441. doi:10.1016/j.jaci.2021.10.001
2. Papi A, Brightling C, Pedersen SE, et al. Asthma. *Lancet*. 2018;391(10122):783–800. doi:10.1016/S0140-6736(17)33311-1
3. Jones TL, Neville DM, Chauhan AJ. Diagnosis and treatment of severe asthma: a phenotype-based approach. *Clin Med*. 2018;18(Suppl 2):s36–s40. doi:10.7861/clinmedicine.18-2-s36
4. Rajvanshi N, Kumar P, Goyal JP. Global Initiative for Asthma Guidelines 2024: an update. *Indian Pediatr*. 2024;61(8):781–786. doi:10.1007/s13312-024-3260-7
5. Bousquet J, Anto JM, Bachert C, et al. Allergic rhinitis. *Nat Rev Dis Primers*. 2020;6(1):95. doi:10.1038/s41572-020-00227-0
6. Huang K, Yang T, Xu J, et al. Prevalence, risk factors, and management of asthma in China: a national cross-sectional study. *Lancet*. 2019;394(10196):407–418. doi:10.1016/S0140-6736(19)31147-X

7. Zhao L, Yang Y, Zang YR, et al. Risk factors for asthma in patients with allergic rhinitis in eastern China. *Am J Otolaryngol*. 2022;43(3):103426. doi:10.1016/j.amjoto.2022.103426
8. Gan H, Luo W, Huang Z, et al. House dust mite components sensitization profile in China, a multi-centre study. *Clin Exp Allergy*. 2023;53(2):226–229. doi:10.1111/cea.14255
9. Durham SR, Shamji MH. Allergen immunotherapy: past, present and future. *Nat Rev Immunol*. 2023;23(5):317–328. doi:10.1038/s41577-022-00786-1
10. Pavón-Romero GF, Parra-Vargas MI, Ramírez-Jiménez F, et al. Allergen immunotherapy: current and future trends. *Cells*. 2022;11(2):212. doi:10.3390/cells11020212
11. Incorvaia C, Cavaliere C, Schroeder JW, et al. Safety and adverse reactions in subcutaneous allergen immunotherapy: a review. *Acta Biomed*. 2023;94(4):e2023172. doi:10.23750/abm.v94i4.14239
12. Bernstein DI, Epstein TG. Safety of subcutaneous allergen immunotherapy. *Allergy Asthma Proc*. 2022;43(4):267–271. doi:10.2500/aap.2022.43.220035
13. McGregor MC, Krings JG, Nair P, et al. Role of biologics in asthma. *Am J Respir Crit Care Med*. 2019;199(4):433–445. doi:10.1164/rccm.201810-1944CI
14. Bakakos A, Loukides S, Usmani OS, et al. Biologics in severe asthma: the overlap endotype - opportunities and challenges. *Expert Opin Biol Ther*. 2020;20(12):1427–1434. doi:10.1080/14712598.2020.1809651
15. Bousquet J, Humbert M, Gibson PG, et al. Real-world effectiveness of omalizumab in severe allergic asthma: a meta-analysis of observational studies. *J Allergy Clin Immunol Pract*. 2021;9(7):2702–2714. doi:10.1016/j.jaip.2021.01.011
16. Tarraf HN, Masoud HH, Zidan M, et al. Effectiveness and safety of omalizumab in severe, persistent IgE-mediated asthma in pediatric and adult patients: a real-world observational study in Egyptian population. *J Asthma*. 2020;57(2):160–166. doi:10.1080/02770903.2018.1553051
17. Kaplan AP, Giménez-Arnau AM, Saini SS. Mechanisms of action that contribute to efficacy of omalizumab in chronic spontaneous urticaria. *Allergy*. 2017;72(4):519–533. doi:10.1111/all.13083
18. Serrano-Candelas E, Martinez-Aranguren R, Valero A, et al. Comparable actions of omalizumab on mast cells and basophils. *Clin Exp Allergy*. 2016;46(1):92–102. doi:10.1111/cea.12668
19. Braido F, Corsico A, Rogkakou A, et al. The relationship between allergen immunotherapy and omalizumab for treating asthma. *Expert Rev Respir Med*. 2015;9(2):129–134. doi:10.1586/17476348.2015.1000866
20. Zhang YY, Zhang M, Zhang JQ, et al. Combination of omalizumab with allergen immunotherapy versus immunotherapy alone for allergic diseases: a meta-analysis of randomized controlled trials. *Int Forum Allergy Rhinol*. 2023.
21. Kathuria PC, Rai M. Omalizumab with allergen immunotherapy in respiratory & food allergy. *Indian J Tuberc*. 2025;72(1):98–102. doi:10.1016/j.ijtb.2024.06.011
22. Bozek A, Kozłowska R, Misiołek M, et al. Omalizumab added to allergen immunotherapy increased the effect of therapy in patients with severe local allergic rhinitis. *Hum Vaccin Immunother*. 2022;18(6):2097818. doi:10.1080/21645515.2022.2097818
23. Shen W, Zhou Q, Zhang Q, et al. Efficacy and safety of omalizumab combined with allergen immunotherapy in children with moderate to severe allergic asthma. *Int Forum Allergy Rhinol*. 2025;15(2):208–211. doi:10.1002/alr.23470
24. Long C, Sun C, Lin H, et al. Efficacy and safety of subcutaneous immunotherapy combined with omalizumab in children with dust mite-induced asthma. *J Asthma*. 2024;61(11):1561–1570. doi:10.1080/02770903.2024.2368193
25. Dantzer JA, Wood RA. Update on omalizumab in allergen immunotherapy. *Curr Opin Allergy Clin Immunol*. 2021;21(6):559–568. doi:10.1097/ACI.0000000000000781
26. Bayar Muluk N, Cingi C. Biologics in allergic rhinitis. *Eur Rev Med Pharmacol Sci*. 2023;27(5 Suppl):43–52. doi:10.26355/eurrev_202310_34069