

Predictors of Omalizumab non-response in ABPA and exploratory biomarkers for switching to mepolizumab: A retrospective cohort study

Huijuan Wang

Beijing Chaoyang Hospital, Capital Medical University

Yangyu Chen

Beijing Chaoyang Hospital, Capital Medical University

Xiaoyan Jing

Beijing Chaoyang Hospital, Capital Medical University

Yining Zhang

Capital Medical University

Kewu Huang

kewuhuang2025@126.com

Beijing Chaoyang Hospital, Capital Medical University

Research Article

Keywords: Allergic bronchopulmonary aspergillosis, Biological therapy, Omalizumab, Mepolizumab, Treatment response

Posted Date: September 30th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10727692/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Omalizumab and mepolizumab are used in treatment-dependent allergic bronchopulmonary aspergillosis (ABPA). This study aimed to identify clinical factors and biomarkers associated with non-response to omalizumab and serological and inflammatory biomarkers that may identify patients who derive clinical benefit from switching to mepolizumab after omalizumab treatment failure.

Methods

A single-center retrospective cohort analysis was performed on 63 ABPA patients who received omalizumab therapy from December 2016 to July 2025 at Beijing Chaoyang hospital. Clinical data of these patients was compared between omalizumab responders (n = 33) and non-responders (n = 30). A small exploratory subgroup of 13 omalizumab non-responders who switched to mepolizumab was compared with 21 patients who maintained stable omalizumab monotherapy. Multivariable regression analysis and Receiver Operating Characteristic (ROC) analysis were used in this study.

Results

Among 63 patients receiving omalizumab, non-responders had a shorter disease duration, higher baseline peripheral eosinophils count, higher Fractional exhaled nitric oxide (FeNO) level, and more frequent mucous plugs than responders. Multivariable regression analysis indicated longer oral corticosteroids (OCS) duration (Odds Ratio (OR) = 1.18 95%CI 1.026–1.358, p = 0.021) and the presence of mucous plugs (OR = 1.731, 95%CI 1.536–5.587, p = 0.012) as independent risk factors for non-response to omalizumab. Longer symptom-to treatment interval was protective against non-response (OR = 0.921, 95%CI 0.895–0.987, P = 0.019). For the exploratory subgroup comparison (21 omalizumab-maintained patients vs 13 patients switched to mepolizumab), the switch group was younger and had higher baseline total IgE, Aspergillus-specific IgE, eosinophils and FeNO. Exploratory ROC analysis identified that baseline FeNO > 47.5 ppb and Aspergillus-specific IgE > 6.995 KU/L yielded an Area Under Curve of 0.850 for potential mepolizumab responsiveness. These cut-off values are only hypothesis-generating due to the limited subgroup sample size.

Conclusion

Specific clinical and biomarker profiles can predict differential responses to omalizumab and mepolizumab in ABPA.

Introduction

Allergic Bronchopulmonary Aspergillosis (ABPA) is a hypersensitivity-mediated destructive lung disorder triggered by repeated airway exposure to *Aspergillus fumigatus*, predominantly complicating severe asthma[1]. Globally, ABPA affects approximately 2.5-5.0% of patients of asthma, with substantially higher prevalence in steroid-dependent asthma[2]. In China, large cohort studies have highlighted the significant clinical burden of ABPA, often characterized by diagnostic delays averaging up to 10 years, leading to irreversible lung damage by the time of diagnosis[3]. The disease manifests with a spectrum of symptoms, including chronic cough, wheezing, expectoration of brownish mucus plugs, and, if untreated, can progress to central bronchiectasis and pulmonary fibrosis, severely impacting quality of life and survival[4].

The pathophysiology of ABPA involves a complex immune response to *Aspergillus fumigatus*, including type I and type III hypersensitivity reactions[5]. Persistent airway irritation caused by the fungus leads to T-helper 2 cell polarization, resulting in elevated total and Aspergillus-specific IgE, eosinophilia, and release of inflammatory cytokines such as IL-4, IL-5, and IL-13[6, 7]. The management of ABPA requires systemic oral corticosteroids (OCS) and/or antifungal medications[8–10]. Systemic corticosteroids is an effective therapy for ABPA patients which can successfully suppress inflammatory response in the first 6 weeks[11]. Antifungal agents are used to reduce fungal burden and have been shown to prolong the time to first exacerbation and reduce corticosteroid requirements[12]. However, long-term OCS administration carries severe systemic toxicities and over half of patients experience recurrent flares during steroid tapering, resulting in steroid dependency[13].

Biologic monoclonal antibodies targeting distinct type 2 inflammatory axes have emerged as second-line agents for refractory ABPA. Omalizumab (anti-IgE) reduces exacerbation frequency, OCS consumption and inflammatory burden in real-world ABPA cohorts[14–16]. Mepolizumab (anti-IL-5) directly suppresses eosinophilic inflammation and demonstrates efficacy in patients failing anti-IgE therapy[17, 18]. Nevertheless, patient treatment response to individual biologics is highly heterogeneous, and validated baseline clinical or serological predictors to guide upfront biologic selection remain unclear. Existing published evidence consists largely of small case series, single-agent efficacy reports, and meta-analyses pooling mixed patient populations

Despite growing evidence supporting the efficacy of biologics, several critical knowledge gaps remain. First, Large real-world Chinese cohorts defining independent baseline predictors of primary omalizumab non-response are lacking. Second, no validation quantitative serological cut-offs exist to stratify patients suitable for sequential switching to mepolizumab after omalizumab failure. Third, few studies systematically compare clinical, serological and radiological phenotypes between patients who maintain omalizumab response and those requiring IL-5 inhibitor rescue therapy.

Therefore, this study establishes a primary analysis of 63 omalizumab-treated ABPA patients to identify independent predictors of omalizumab treatment failure. As a secondary exploratory analysis, we compare baseline profiles between stable omalizumab responders and a smaller cohort of patients

switched to mepolizumab, generating preliminary biomarker cut-offs to inform future prospective validation studies.

Methods

Data source and Ethical approval

This was a retrospective cohort study conducted at a single center. The study was designed to analyze the clinical characteristics and treatment responses of patients diagnosed with ABPA who were treated with biologic agents, specifically omalizumab and mepolizumab from December 2016 to July 2025 in Beijing Chaoyang hospital. The study protocol was by Ethics Committee of Beijing chao-yang hospital (2025-ke-347) and additional informed consent was waived for the retrospective cohort.

Study Population and Patient Selection

All patients with a confirmed ABPA diagnosis per 2024 International Society for Human and Animal Mycology (ISHAM) working group diagnostic criteria were screened from institutional electronic medical records. Patient inclusion criteria were as follows: (1) Aged ≥ 18 years at biologic initiation. (2) Definite ABPA diagnosis consistent with ISHAM 2024 criteria[9]. (3) Minimum 6 consecutive months of omalizumab therapy with complete baseline clinical and serological data at biologic initiation. (4) Minimum 12 months of post-biologic follow-up data for response classification. Exclusion criteria were as follows: (1) Incomplete electronic medical records missing core baseline or follow-up endpoints. (2) Follow-up duration shorter than 12 months after biologic commencement. (3) Concomitant treatment with two or more biologics simultaneously at baseline.

Clinical Data Extraction and Variable Definitions

Clinical baseline data were extracted from the electronic medical records at the time of ABPA diagnosis. Clinical Characteristics and Comorbidities including age, sex, time from onset to initial treatment, underlying respiratory diseases, and presence of sinusitis or allergic rhinitis were recorded. Baseline serum total IgE levels, *Aspergillus fumigatus*-specific IgE levels, *Aspergillus*-specific IgG levels, peripheral blood eosinophil count, and fractional exhaled nitric oxide (FeNO) levels. IgE levels were measured using immunoassay techniques, such as the ImmunoCAP system.

Chest high-resolution computed tomography (HRCT) scans were independently reviewed by two thoracic radiologists. Radiological endpoints recorded included presence of central bronchiectasis and high-attenuation mucous plugging. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and the FEV1/FVC ratio were measured according to American Thoracic Society/European Respiratory Society guidelines. Complete spirometry data were only available for a subset of participants and missing lung function data are acknowledged as an inherent retrospective limitation.

Biologic Treatment Protocols

All patients received background maintenance therapy with high-dose inhaled corticosteroids plus long-acting β 2-agonists prior to biologic initiation. The treatment protocol involved the administration of omalizumab according to standard dosing regimens based on serum total IgE levels and body weight. For these ABPA patients whose body weight or total IgE fell outside the standard dosing table were given the dose of 600mg every 2 weeks. Patients switched to mepolizumab received 100 mg subcutaneously administered every 4 weeks following confirmed omalizumab treatment failure.

The definition of treatment response was based on a composite of clinical, serological, and functional improvements (aligned with 2024 ISHAM ABPA guidance). Response to omalizumab was defined as a reduction in OCS requirement by greater than or equal to 50% from baseline, absence of acute exacerbations for at least 6 months, and improvement in respiratory symptoms.

Biologic therapy non-response was defined as failure to reduce OCS dose by 50%, persistent refractory respiratory symptoms, or radiological progression despite at least 6 months of omalizumab therapy [15]. ABPA patients in no-response group, those who were subsequently switched to mepolizumab responded were considered as another subgroup. Then we compared the baseline clinical data between the two subgroups. ABPA acute exacerbation was defined as a worsening of respiratory symptoms requiring systemic corticosteroids or hospitalization, accompanied by a greater than or equal to 50% increase in total IgE from the baseline stable value.

Subgroup Analysis

Primary analysis cohort: All patients receiving omalizumab, split into responders and non-responders. Univariable and multivariable logistic regression models were constructed to identify independent predictors of omalizumab non-response.

Secondary exploratory subgroup: Within the omalizumab cohort, patients with sustained clinical response maintained long-term omalizumab monotherapy. Omalizumab non-responders underwent sequential switch to mepolizumab. Baseline clinical and serological profiles were compared between these two subgroups. ROC curve analysis was performed for biomarker cut-off generation. All ROC results are labelled exploratory due to the small sample size and limited statistical power.

Statistical Analysis

All statistical analysis was performed using SPSS Version 27.0. Normality testing was completed via Shapiro-Wilk test. Normally distributed continuous variables are reported as mean $\pm$ standard deviation (SD). Non-normal continuous variables are presented as median (interquartile range, IQR). Categorical variables are summarized as count (percentage). Between-group comparisons for continuous variables used independent samples t-test (normal distribution) or Mann-Whitney U test (non-normal distribution). Categorical variable comparisons utilized Chi-squared test. For logistic regression: all univariable variables with $p < 0.05$ were entered into a multivariable forward conditional logistic regression model to calculate adjusted odds ratios (OR) and 95% confidence intervals (CI). ROC curve analysis calculated

AUC and optimal cut-off values maximising combined sensitivity and specificity. A two-tailed p-value <0.05 was defined as statistically significant for primary cohort comparisons.

Results

Patient selection and classification

A total of 265 ABPA patients were screened from December 2016 and July 2025. 32 patients were excluded due to loss to follow-up or missing clinical data. Of the remaining 233 patients, 163 were treated without biologic therapy. The final analysis focused on the 70 patients who received biologic therapy. This group consisted of 63 patients treated with omalizumab, 4 with mepolizumab, and 3 with dupilumab. Among these 63 ABPA patients, we compared clinical characteristics between ABPA patients who responded to omalizumab (N=33) and those who did not (N=30). The secondary exploratory subgroup comparison included 21 stable omalizumab responders and 13 patients switched to mepolizumab after omalizumab failure (**Figure 1**).

Clinical Data Comparison Between Omalizumab Responders and Non-Responders

Between the responders and non-responders in ABPA patients treated with omalizumab, there were no significant differences in baseline demographics, including sex, age, or underlying comorbidities such as asthma, COPD, bronchiectasis, and sinusitis/allergic rhinitis. Significant differences were observed in several key clinical characteristics. The duration from symptom onset to initial treatment was significantly longer in responders (15 years) compared to non-responders (4.5 years, $p=0.010$). Non-responders had a significantly higher baseline blood eosinophil count (0.65 vs. $0.2 \times 10^9/L$, $p=0.015$) and higher FeNO levels (47.5 vs. 27 ppb, $p=0.015$). Furthermore, non-responders required a significantly longer duration of OCS treatment (12 vs. 8 months, $p=0.010$), although the baseline OCS dose was not significantly different. No significant differences were found in baseline total IgE, Aspergillus-specific IgE, Aspergillus-specific IgG, lung function parameters (FEV1% predicted, FEV1/FVC), or microbiology findings. These findings suggest that a shorter disease history, more intense type 2 inflammation, and the presence of mucous plugs may be associated with a poorer response to omalizumab in this patient cohort (**Table 1**).

Multivariable logistic regression analysis for omalizumab Non-response

Then, these significantly different indicators were included into multivariable logistic regression analysis. Results showed that longer duration of OCS treatment (OR 1.180, 95% CI 1.026-1.358; $p=0.021$) and the presence of mucous plugs on imaging (OR 1.731, 95% CI 1.536-5.587; $p=0.012$) were identified as independent risk factors of omalizumab treatment failure. Conversely, a longer time from symptom onset to initial treatment was a negative predictor (OR 0.921, 95% CI 0.895-0.987; $p=0.019$). Baseline eosinophil count and FeNO lost independent predictive significance after multivariable adjustment ($p>0.05$) (**Table 2**).

Omalizumab-Maintained Responders vs Mepolizumab Switch Subgroup

Among these 63 ABPA patients, we compared clinical characteristics between ABPA patients responsive to omalizumab plus maintenance oral corticosteroids (mOCS) (N=21) and those who required a switch from omalizumab to mepolizumab and responded (N=13). Patients who switched to mepolizumab were younger (47 vs. 62 years, $p<0.001$) and had a shorter time from symptom onset to initial treatment (3 vs. 8 years, $p<0.001$). The switch group exhibited significantly higher baseline inflammatory markers, including total IgE (1410 vs. 1313 IU/L, $p=0.044$), Aspergillus-specific IgE (14.1 vs. 13.7 KU/L, $p=0.022$), blood eosinophil count (1.41 vs. $0.25 \times 10^9/L$, $p<0.001$), and FeNO levels (83 vs. 28 ppb, $p=0.005$). There were no significant differences in the prevalence of underlying diseases, microbiology results, or baseline lung function between the two groups (**Table 3**). The ROC analysis identified two significant biomarkers for predicting a better response to mepolizumab over omalizumab. A baseline FeNO level greater than 47.5 ppb and a baseline Aspergillus-specific IgE (sIgE) level greater than 6.995 KU/L were significant predictors, each with an AUC of 0.850. The sIgE cut-off showed perfect specificity (100%) and high sensitivity (80%) for identifying potential mepolizumab responders. In contrast, total IgE and blood eosinophil counts did not show significant predictive value in this analysis (**Table 4**). Consistent with study limitations, these cut-offs are not validated for standalone clinical use and require replication in larger independent cohorts.

Discussion

This single-center Chinese real-world cohort of 63 omalizumab-treated ABPA patients represents one of the largest real-world cohorts of omalizumab-treated ABPA patients in China. This study identified mucous plugs and a shorter time from symptom onset to initial treatment linked to poor omalizumab response and proposes FeNO/sIgE cut-offs to predict better outcomes with mepolizumab. These findings provide a testable hypothesis for the selection of biologic therapy in treatment-dependent patients with ABPA.

Mucous plugging has previously been associated with poor biologic efficacy in international ABPA cohorts[19]. Our multivariable model confirms radiological mucous plugging as a robust independent predictor of omalizumab non-response, consistent with a 2025 real-world ABPA analysis by Carter et al. that identified mucus plugging as the sole radiological phenotype linked to universal biologic treatment failure [17]. Mucous plugs in airway can cause local hypoxia, where *P aeruginosa* survived and in the absence of oxygen by being supplied with energy [20, 21]. Mucous plugs are not merely a consequence of inflammation but actively contribute to disease persistence. They create a physical barrier that impedes drug penetration to the airway mucosa, foster a microenvironment for fungal persistence. The presence of these plugs could physically limit the access of biologics to their targets of action, explaining the suboptimal response to omalizumab. Another important finding of this study was that the earlier intervention cohort had poorer outcomes with anti-IgE therapy. This suggests that these patients have a more aggressive or severe disease phenotype from the onset. Age at onset of ABPA < 50 years was also a risk factor of difficult-to-treat ABPA patients with an OR of 3.8[22].

The subgroup of 13 patients switched to mepolizumab after omalizumab failure exhibited a severe hyper-type 2 endotype characterized by markedly elevated Aspergillus sIgE, FeNO and peripheral eosinophils. These biomarkers are cornerstones of ABPA pathogenesis. IgE plays a central role in the immediate hypersensitivity reaction to Aspergillus antigens[23, 24], while eosinophils and FeNO are indicative of IL-5-driven inflammation and IL-4/IL-13-mediated epithelial activation[25]. Patients in non-response group who eventually switched from omalizumab to mepolizumab were younger and presented with a significantly shorter duration from symptom onset to initial treatment, which was consistent with previous study[22].

Exploratory ROC analysis identified FeNO and Aspergillus sIgE quantitative cut-offs with strong discriminatory capacity. However, critical limitations of this small exploratory subgroup must be emphasized. With only 13 switch patients, statistical power is insufficient to establish definitive clinical thresholds, and these values cannot be recommended for routine clinical decision-making without external multi-center validation. Prior published reports of sequential biologic switching in ABPA are limited to individual case reports and tiny case series; this study provides the first quantitative biomarker reference frame, albeit preliminary, for stratifying candidates for IL-5 inhibitor rescue therapy.

Limitations

Several limitations of this study must be acknowledged. First, Single-center retrospective design introduces inherent selection bias and unmeasured confounding variables related to local treatment pathways and referral patterns. Multi-center prospective cohorts are required to confirm these results. Second, the exploratory mepolizumab-switch subgroup comprises only 13 patients, substantially limiting statistical power and precluding definitive clinical inference from ROC-derived biomarker cut-offs. Third, complete baseline and follow-up HRCT and spirometry data were unavailable for all enrolled participants. No external validation cohort was available to test the predictive performance of the identified biomarkers for omalizumab non-response and mepolizumab suitability. Fourth, serial longitudinal monitoring of inflammatory biomarkers (tIgE, eosinophils, FeNO) during biologic therapy was not uniformly captured across all patients, prohibiting dynamic trajectory analysis of treatment response.

For routine ABPA clinical practice, baseline HRCT screening for airway mucous plugging and review of cumulative prior oral corticosteroid duration provide simple, low-cost tools to identify patients at high risk of primary omalizumab failure. For young patients presenting with markedly elevated FeNO and Aspergillus sIgE at diagnosis, upfront consideration of IL-5-targeted biologic therapy (rather than initial omalizumab) may reduce rates of sequential treatment switching and prolonged OCS dependency, pending prospective validation of our exploratory biomarker thresholds. Large multi-center prospective Chinese ABPA cohorts are required to externally validate the independent predictors of omalizumab non-response and refine the FeNO/Aspergillus sIgE cut-offs for mepolizumab rescue eligibility. Further work should compare head-to-head efficacy of first-line omalizumab versus mepolizumab stratified by baseline type 2 inflammatory endotypes, and evaluate combined sequential biologic regimens for ultra-

refractory ABPA phenotypes. Longitudinal serial biomarker monitoring will help define dynamic response thresholds during biologic maintenance therapy.

Conclusions

This single-centre retrospective cohort of 63 Chinese adults with ABPA demonstrates that baseline radiological mucous plugging and prolonged prior oral corticosteroid exposure independently predict poor clinical response to omalizumab. An exploratory subgroup analysis of 13 patients switching to mepolizumab after omalizumab failure identifies elevated baseline FeNO (> 47.5 ppb) and Aspergillus-specific IgE (> 6.995 KU/L) as candidate predictive biomarkers for IL-5 inhibitor rescue benefit. All biomarker thresholds derived from the small mepolizumab-switch subgroup require validation in larger independent patient cohorts before implementation into clinical ABPA treatment algorithms.

Abbreviations

ABPA, Allergic Bronchopulmonary Aspergillosis; CF, cystic fibrosis;

OCS, oral corticosteroids; ISHAM, International Society for Human and Animal Mycology; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation; CI, confidence intervals;

OR, odds ratios; ROC, Receiver Operating Characteristic curve; AUC, area under curve.

Declarations

Ethics approval and consent to participate

The study protocol was by Ethics Committee of Beijing chao-yang hospital (2025-ke-347) and additional informed consent was waived for the retrospective cohort.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

This study was supported by national Science and Technology Major Project (ID:2024ZD0529804).

Authors' contributions

XYJ and YNZ analyzed and interpreted the patient data regarding the ABPA. HJW and YYC performed statistical analysis, and were the major contributor in writing the manuscript. KWH supervised and revised the first draft of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Chen H, Zhang X, Zhu L, An N, Jiang Q, Yang Y, Ma D, Yang L, Zhu R: Clinical and immunological characteristics of *Aspergillus fumigatus*-sensitized asthma and allergic bronchopulmonary aspergillosis. *Front Immunol* 2022, 13:939127.<http://doi.org/10.3389/fimmu.2022.939127>.
2. Denning DW, Pleuvry A, Cole DC: Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol* 2013, 51(4):361-370.<http://doi.org/10.3109/13693786.2012.738312>.
3. Zhang X, Xu Y, Wang M, Chen L, Wang Q, Zhu X, Li H, Wang S, Jiang H: The association between different regimens of glucocorticoid and antifungal treatment with the prognosis of allergic bronchopulmonary aspergillosis: a retrospective cohort study. *Ann Med* 2026, 58(1):2612394.<http://doi.org/10.1080/07853890.2025.2612394>.
4. He Q, Li M, Cao J, Zhang M, Feng C: Clinical characteristics and risk factors analysis of allergic bronchopulmonary aspergillosis combined with bronchiectasis. *Front Med (Lausanne)* 2025, 12:1557241.<http://doi.org/10.3389/fmed.2025.1557241>.
5. Agarwal R, Muthu V, Sehgal IS: Clinical Manifestation and Treatment of Allergic Bronchopulmonary Aspergillosis. *Semin Respir Crit Care Med* 2024, 45(1):114-127.<http://doi.org/10.1055/s-0043-1776912>.
6. Shankar J, Thakur R, Clemons KV, Stevens DA: Interplay of Cytokines and Chemokines in Aspergillosis. *J Fungi (Basel)* 2024, 10(4).<http://doi.org/10.3390/jof10040251>.
7. Wu G, Meng X, Zheng P, Zhang XD, Li L, Hu H, Sun B: Elevated serum levels of periostin in patients with allergic bronchopulmonary aspergillosis. *Mycoses* 2019, 62(9):780-789.<http://doi.org/10.1111/myc.12957>.
8. Agarwal R, Khan A, Aggarwal AN, Saikia B, Gupta D, Chakrabarti A: Role of inhaled corticosteroids in the management of serological allergic bronchopulmonary aspergillosis (ABPA). *Intern Med* 2011, 50(8):855-860.<http://doi.org/10.2169/internalmedicine.50.4665>.
9. Agarwal R, Sehgal IS, Muthu V, Denning DW, Chakrabarti A, Soundappan K, Garg M, Rudramurthy SM, Dhooria S, Armstrong-James D et al: Revised ISHAM-ABPA working group clinical practice

- guidelines for diagnosing, classifying and treating allergic bronchopulmonary aspergillosis/mycoses. *Eur Respir J* 2024, 63(4).<http://doi.org/10.1183/13993003.00061-2024>.
10. Agarwal R, Muthu V, Sehgal IS, Dhooria S, Prasad KT, Garg M, Aggarwal AN, Chakrabarti A: A randomised trial of prednisolone versus prednisolone and itraconazole in acute-stage allergic bronchopulmonary aspergillosis complicating asthma. *Eur Respir J* 2022, 59(4).<http://doi.org/10.1183/13993003.01787-2021>.
 11. Agarwal R, Dhooria S, Singh Sehgal I, Aggarwal AN, Garg M, Saikia B, Behera D, Chakrabarti A: A Randomized Trial of Itraconazole vs Prednisolone in Acute-Stage Allergic Bronchopulmonary Aspergillosis Complicating Asthma. *Chest* 2018, 153(3):656-664.<http://doi.org/10.1016/j.chest.2018.01.005>.
 12. Francis NZ, Southern KW: Antifungal therapies for allergic bronchopulmonary aspergillosis in people with cystic fibrosis. *Cochrane Database Syst Rev* 2022, 9(9):CD002204.<http://doi.org/10.1002/14651858.CD002204.pub5>.
 13. Joest M, Klein J, Kutting D, Skowasch D: [Allergic bronchopulmonary aspergillosis (ABPA) - an Update]. *Pneumologie* 2024, 78(3):204-214.<http://doi.org/10.1055/a-1854-3006>.
 14. Chen P, Yu Y, He L, Zhang C, Li Y, Wu D, Chen Y, Wang R, Xu G, Cao C: Efficacy of omalizumab in adult patients with allergic bronchopulmonary aspergillosis: a multicentre study in China. *Clin Exp Med* 2024, 24(1):6.<http://doi.org/10.1007/s10238-023-01267-y>.
 15. Jin M, Douglass JA, Elborn JS, Agarwal R, Calhoun WJ, Lazarewicz S, Jaumont X, Yan M: Omalizumab in Allergic Bronchopulmonary Aspergillosis: A Systematic Review and Meta-Analysis. *J Allergy Clin Immunol Pract* 2023, 11(3):896-905.<http://doi.org/10.1016/j.jaip.2022.12.012>.
 16. Perez-de-Llano LA, Vennera MC, Parra A, Guallar J, Marin M, Asensio O, Ausin P, Borderias L, Fernandez C, Granel C et al: Effects of omalizumab in Aspergillus-associated airway disease. *Thorax* 2011, 66(6):539-540.<http://doi.org/10.1136/thx.2010.153312>.
 17. Carter C, Torre IB, Blackburn S, Nwankwo L, Semple T, Rawal B, Armstrong-James D, Patel PH, Shah A: Real-World Effectiveness of Biologic Therapy in Allergic Bronchopulmonary Aspergillosis. *J Allergy Clin Immunol Pract* 2025, 13(5):1094-1102 e1091.<http://doi.org/10.1016/j.jaip.2025.03.006>.
 18. Li X, Liu P, Gao T, Wang J, Wu M, Li H, Qu Y, Du R, Dong L, Qi Q et al: Effectiveness and Safety of Mepolizumab in Allergic Bronchopulmonary Aspergillosis (ABPA): Real-World Experience From a Chinese Retrospective Case Series. *Clin Exp Allergy* 2025.<http://doi.org/10.1111/cea.70199>.
 19. Nomura N, Matsumoto H, Asano K, Hayashi Y, Yokoyama A, Nishimura Y, Hashimoto N, Sakagami T, Fukunaga K, Hizawa N et al: Refractory phenotype of Aspergillus-sensitized asthma with bronchiectasis and allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol Glob* 2025, 4(1):100364.<http://doi.org/10.1016/j.jacig.2024.100364>.
 20. Boucher RC: Muco-Obstructive Lung Diseases. *N Engl J Med* 2019, 380(20):1941-1953.<http://doi.org/10.1056/NEJMr1813799>.
 21. Cowley ES, Kopf SH, LaRiviere A, Ziebis W, Newman DK: Pediatric Cystic Fibrosis Sputum Can Be Chemically Dynamic, Anoxic, and Extremely Reduced Due to Hydrogen Sulfide Formation. *mBio*

- 2015, 6(4):e00767.<http://doi.org/10.1128/mBio.00767-15>.
22. Tanaka J, Oguma T, Ishiguro T, Taniguchi H, Nishiuma T, Tateno H, Matsumoto H, Koshimizu N, Ito Y, Matsunaga K et al: Clinical Characteristics of Difficult-To-Treat Allergic Bronchopulmonary Aspergillosis and Its Prediction Score. *Allergy* 2025, 80(9):2531-2540.<http://doi.org/10.1111/all.16559>.
23. Kuwabara K, Hirose M, Kato K, Yokoi T, Shiga M, Kondo R, Nakamura M, Matsunaga K, Horiguchi T: Serological analysis of sensitization in allergic bronchopulmonary aspergillosis: a study on allergen components and interspecies relationships. *J Asthma* 2020, 57(6):610-617.<http://doi.org/10.1080/02770903.2019.1599387>.
24. Koundal P, Manhas S, Aman S, Haque S, Singh B, Mohammed SA, Oellerich M, Tuli HS, Ramniwas S, Dangi M et al: Pathogen-specific IgE-reactive cytosolic allergenic epitopes of *Aspergillus fumigatus* for immunodiagnostic/immunotherapeutic applications against allergic aspergillosis. *Ann Clin Microbiol Antimicrob* 2026, 25(1):7.<http://doi.org/10.1186/s12941-025-00846-z>.
25. Dietschmann A, Schrufer S, Westermann S, Henkel F, Castiglione K, Willebrand R, Adam J, Ruland J, Lang R, Sheppard DC et al: Phosphatidylinositol 3-Kinase (PI3K) Orchestrates *Aspergillus fumigatus*-Induced Eosinophil Activation Independently of Canonical Toll-Like Receptor (TLR)/C-Type-Lectin Receptor (CLR) Signaling. *mBio* 2022, 13(4):e0123922.<http://doi.org/10.1128/mbio.01239-22>.

Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures

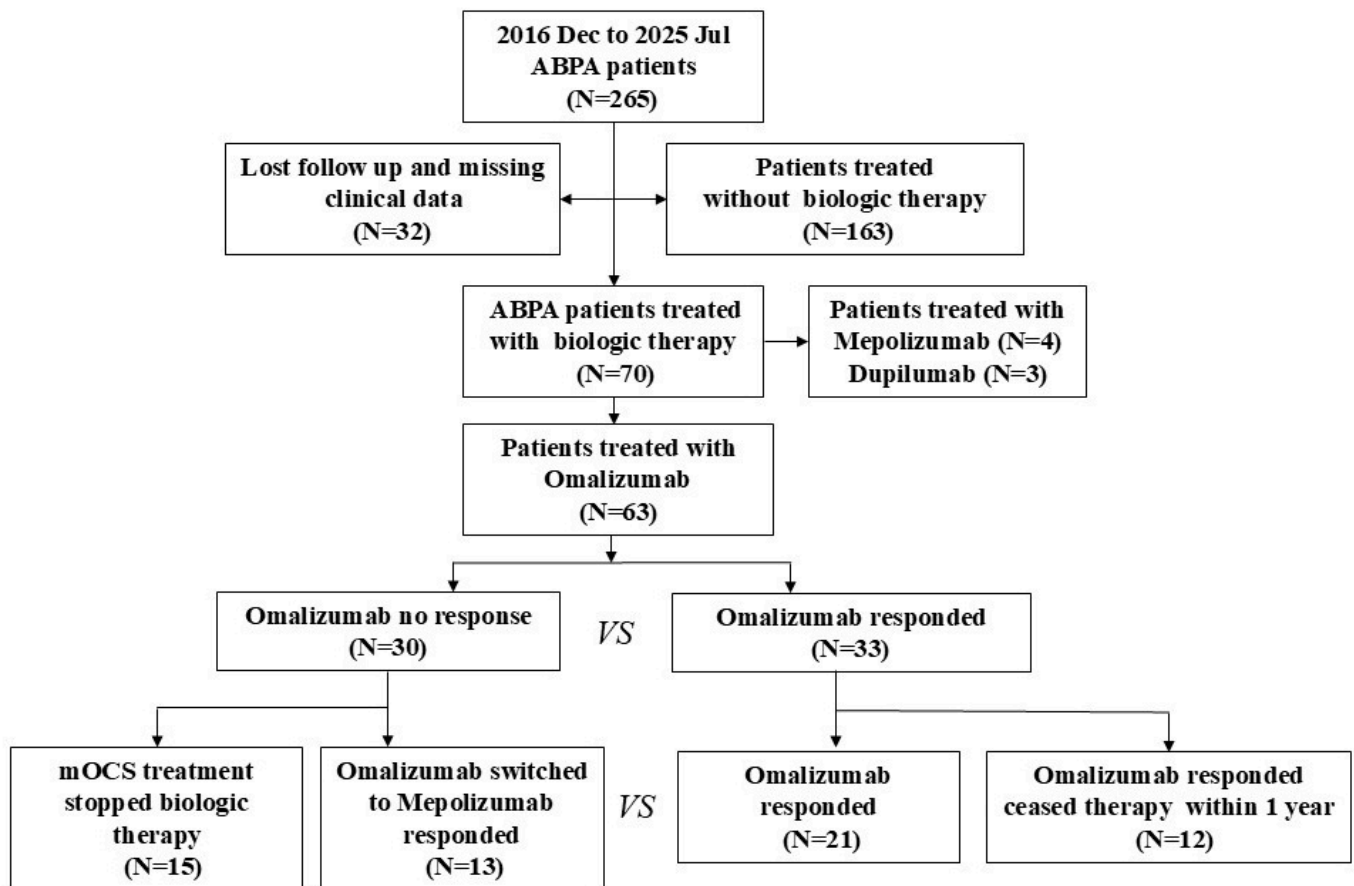


Figure 1

CONSORT-style patient screening flowchart for biologic-treated ABPA cohort. ABPA: Allergic Bronchopulmonary Aspergillosis; OCS: Oral Corticosteroids.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1to4.docx](#)