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RELATIONSHIP BETWEEN EFFECTIVENESS AND VARIATIVENESS OF BRONCHIAL ASTHMA MEDICATION WITH CLINICAL IMPROVEMENT OF BRONCHIAL ASTHMA

Natalia Kristina Br Sinaga
Faculty of Military Pharmacy, Defense University of the Republic of Indonesia, Bogor, Indonesia
Email :natalnat234@gmail.com

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Abstract
Background: Bronchial asthma is a chronic inflammatory airway disease that is highly heterogeneous, both in terms of pathophysiology and response to therapy. The availability of various drug classes ranging from inhaled corticosteroids (ICS), bronchodilators, allergen immunotherapy (AIT), to various biologic agents does not necessarily guarantee uniform clinical improvement in every patient due to variability in endotypes, biomarkers, and treatment adherence. Objective: This review aims to analyze the relationship between the effectiveness and variability of various bronchial asthma drug classes with clinical improvement outcomes, including reduced exacerbations, improved lung function, and quality of life. Methods: A narrative literature review was compiled based on three main articles on allergen immunotherapy, targeted biologic therapy, and tezepelumab in severe asthma, supplemented by additional literature searches on therapy adherence and predictive biomarkers. Results and discussion: The effectiveness of conventional pharmacotherapy is strongly influenced by variability in patient adherence, with the average objective adherence to ICS ranging from 22 - 70% of the prescribed dose. Allergen immunotherapy has demonstrated consistent preventive and therapeutic effects in mild-moderate allergic asthma, but its benefits depend on dose, duration, and patient phenotype. Biologic therapy (anti-IgE, anti-IL-5/IL-5Rα, anti-IL-4Rα) significantly reduced exacerbations, particularly in the type 2-high phenotype with eosinophilia, while tezepelumab, a TSLP inhibitor, demonstrated efficacy across phenotypes, including type 2-low, with annual exacerbation reductions of up to 56–71%. This variability in response underscores the need for biomarker-guided approaches and combination therapies to optimize clinical improvement. Conclusion: The effectiveness of bronchial asthma medications is closely linked to the variability of disease endotypes, patient biomarkers, and therapy adherence; optimal clinical improvement is achieved through a personalized approach based on phenotypes and biomarkers, rather than a single, uniform treatment strategy.

Keywords: *Bronchial Asthma; Drug Effectiveness; Therapy Variability; Allergen Immunotherapy; Biologic Therapy; Tezepelumab; Clinical Improvement*

INTRODUCTION

Bronchial asthma is a chronic inflammatory disease of the airways that affects approximately 300-358 million people worldwide and is a significant public health burden, both in terms of morbidity, quality of life, and health care costs (Vărut et al., 2025; Bonnesen et al., 2023). This disease is characterized by bronchial hyperresponsiveness, airway inflammation, mucus-induced obstruction, and airway wall remodeling that manifests as shortness of breath, wheezing, coughing, and chest tightness (Batard et al., 2025). The heterogeneity of asthma has long been recognized, so that in recent decades the concept of endotypes and phenotypes has emerged, such as allergic asthma, eosinophilic asthma, type 2-high asthma, and type 2-low asthma, each of which has a different immunological mechanism and pattern of therapy response (Batard et al., 2025; Vărut et al., 2025).

Conventional asthma management relies on inhaled corticosteroids (ICS), either alone or in combination with a long-acting beta-2 agonist (LABA), as first-line therapy according to the Global Initiative for Asthma (GINA) guidelines. However, approximately 3–13% of asthma patients experience

severe forms of the disease that are uncontrolled despite high-dose therapy, and this group accounts for more than half of the overall asthma-related economic burden (Batard et al., 2025; Vărut et al., 2025). The failure of conventional therapies in some of these patients has led to the development of various additional modalities, ranging from disease-modifying allergen immunotherapy (AIT) to various biologic agents targeting specific cytokines or inflammatory pathways such as IgE, interleukin-5 (IL-5), interleukin-4/13 (IL-4/13), and most recently, thymic stromal lymphopoietin (TSLP) (Vărut et al., 2025; Mansour et al., 2026).

A fundamental issue that arises is that the availability of a variety of drug options does not automatically result in uniform clinical improvement in every patient. The effectiveness of a drug in controlled clinical trials often differs from its effectiveness in real-world practice, and inter-individual variability in response is influenced by many factors, including the underlying inflammatory endotype, biomarker levels (blood eosinophils, total IgE, fractional exhaled nitric oxide/FeNO), and patient adherence to the prescribed therapy regimen (Jensen et al., 2021; Rackow et al., 2025; Bonnesen et al., 2023). Therefore, understanding the relationship between the effectiveness and variability of asthma medications and clinical improvement outcomes is crucial, both for the development of more precise therapeutic strategies and for day-to-day clinical decision-making.

This literature review was compiled to comprehensively analyze how the variability of bronchial asthma drug classes, ranging from conventional pharmacotherapy, allergen immunotherapy, to various generations of biologic therapy related to the level of effectiveness and clinical improvement achieved, by highlighting the role of biomarkers and patient characteristics as determining factors of this response variability.

Method

This review was compiled using a narrative literature review approach. Three primary scientific articles served as initial references:

(1) a systematic review of allergen immunotherapy in the prevention and treatment of asthma published in Clinical & Experimental Allergy in 2025 (Batard et al., 2025);
(2) a review of targeted biologic therapies in severe asthma published in Pharmaceuticals in 2025 (Vărut et al., 2025);
(3) a review of tezepelumab as a TSLP inhibitor in severe asthma published in Frontiers in Pharmacology in 2026 (Mansour et al., 2026).

To complement and strengthen the analysis, a supplementary literature search was conducted through PubMed, PubMed Central (PMC), and other academic search engines using combination keywords such as "asthma medication adherence," "precision medicine asthma biomarker," and "treatment response heterogeneity asthma." Articles selected as supplementary sources were English-language articles, published in peer-reviewed journals, and relevant to the topic of therapy adherence and predictive biomarkers of asthma treatment response (Jensen et al., 2021; Rackow et al., 2025; Bonnesen et al., 2023). Data extracted from each source included the type of drug or intervention, study population, effectiveness outcomes (reduction in annual exacerbation rate, improvement in forced expiratory volume in the first second/FEV1, improvement in asthma control score), and factors influencing response variability. Synthesis was conducted narratively and thematically, categorized by therapy category, to illustrate patterns of association between drug variability and clinical outcomes.

Results and Discussion

Variability of Response to Conventional Pharmacotherapy and the Role of Adherence

Inhaled corticosteroids remain the backbone of asthma management due to their ability to suppress airway inflammation. However, the effectiveness of ICS in real-world practice varies significantly compared to the results of controlled clinical trials, primarily due to differences in patient adherence. A Danish study comparing self-reported adherence with objective adherence based on prescription

collection data found that approximately 87.6% of patients reported perfect adherence (Foster score of 100%), whereas the average objective adherence, calculated using the medication possession ratio, was only about 54% (Jensen et al., 2021). This significant gap between perceived adherence and actual adherence explains why some patients continue to experience uncontrolled symptoms despite "perceiving" they are taking their therapy as prescribed.

A recent review of asthma medication adherence optimization confirms that adherence is multifactorial, encompassing individual factors (age, medication beliefs), social factors, and healthcare factors, including patient and caregiver mental health, which influence clinical outcomes (Rackow et al., 2025). Interventions tailored to specific patient barriers, supported by digital technology for remote monitoring, have been shown to improve adherence and, in turn, asthma control (Rackow et al., 2025). These findings indicate that variability in the effectiveness of conventional medications is not solely due to differences in the pharmacodynamics of the drugs themselves, but also to variability in patient medication-taking behavior, an aspect often overlooked when medication effectiveness is assessed solely from randomized controlled clinical trial data.

Effectiveness and Variability of Allergen Immunotherapy in Allergic Asthma

In contrast to conventional pharmacotherapy and biologics, which suppress symptoms during therapy, allergen immunotherapy (AIT) is the only disease-modifying modality that provides long-term clinical benefits even after therapy is discontinued (Batard et al., 2025). A review by Batard and colleagues summarized evidence from over 1,700 patients in prospective clinical trials and over 840,000 patients in real-world retrospective database studies, showing that AIT consistently reduces the risk of developing asthma in patients with allergic rhinitis, with risk reductions ranging from 20% to 40% depending on the definition of asthma onset used and the route of administration (subcutaneous or sublingual).

Variability in the effectiveness of AIT is evident depending on several factors: the type of source allergen (seasonal pollens generally show a more consistent preventive effect than perennial allergens), the route of administration (sublingual administration with natural extracts has been shown in some studies to provide greater risk reduction than subcutaneous administration with allergens), the duration of therapy (optimal benefit generally requires at least three years of therapy), and the dose of allergen extract administered (Batard et al., 2025). In the context of the established treatment of mild-moderate allergic asthma, six post-2005 randomized, double-blind, placebo-controlled clinical trials involving over 2,500 patients showed that the benefit of AIT on improving bronchial provocation tests, symptoms, and medication requirements was only significant when the dose of extract administered was sufficiently high in one of the trials, with the steroid-sparing effect being seen only in the highest dose group (18,000 TU), not at lower doses (Batard et al., 2025). This confirms that among the various AIT preparations in circulation, differences in dosage and active allergen content are the main determinants of the variability in effectiveness, so that drugs with the same generic name do not necessarily provide equivalent clinical effectiveness if the effective dosage is different.

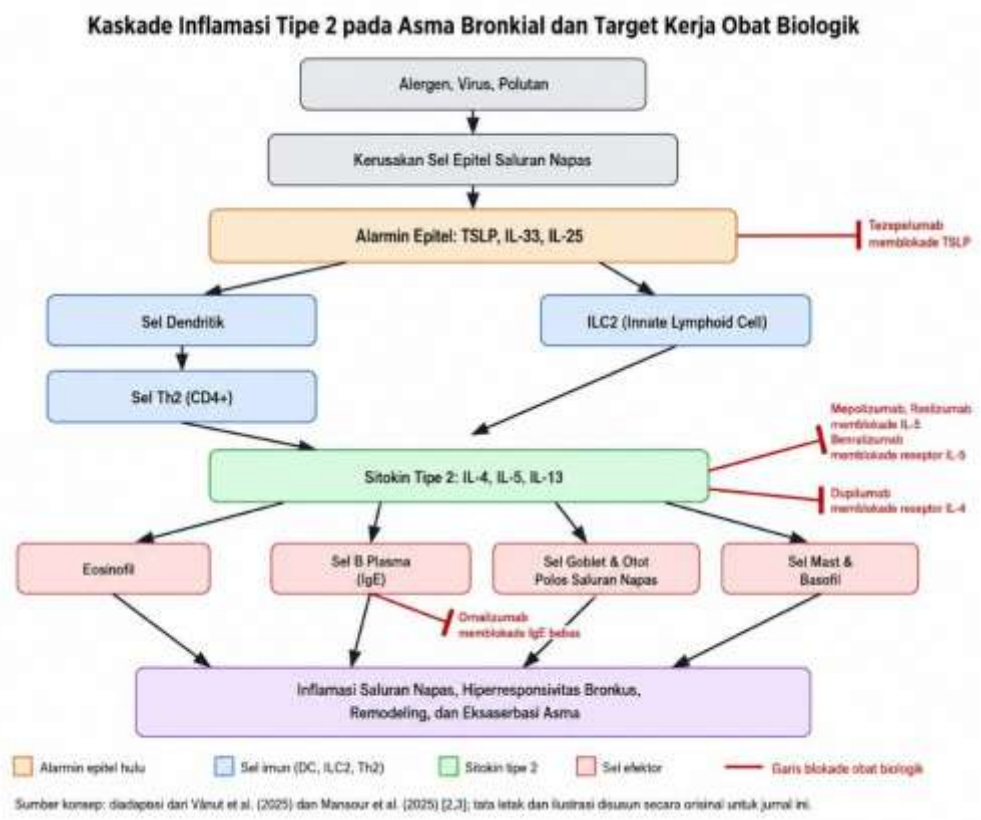
In patients with severe allergic asthma who were previously ineligible for AIT due to the risk of systemic reactions, the combination of AIT with biologics (particularly omalizumab) has been shown to safely expand the indications for AIT. Of the 13 combination studies reviewed, the majority reported that pretreatment with biologics enabled the initiation and continuation of AIT in patients with uncontrolled moderate-to-severe allergic asthma, including those previously unable to tolerate AIT alone (Batard et al., 2025). In a multicenter randomized study, the combination of omalizumab and subcutaneous immunotherapy significantly reduced systemic reactions to AIT (14% versus 26% in the placebo group) and enabled more patients to achieve the target maintenance dose (87% versus 72%) (Batard et al., 2025). These findings demonstrate that drug diversity, in this case, combining two different mechanisms of action, can significantly improve the safety and effectiveness of therapy compared to single modalities.

Effectiveness of Biologic Therapy and Response Variability Based on Endotype

The biologic era began in the early 2000s with the approval of omalizumab (anti-IgE), and has since rapidly expanded into several classes of drugs with different molecular targets: anti-IgE (omalizumab), anti-IL-5/IL-5Rα (mepolizumab, reslizumab, benralizumab, and the newer generation depemokimab), and anti-IL-4Rα that blocks both IL-4 and IL-13 signaling (dupilumab) (Vărut et al., 2025). A review by Vărut and colleagues confirmed that the effectiveness of each of these biologic classes is highly dependent on the patient's baseline biomarker profile, such that variability in response to therapy essentially reflects variability in the underlying inflammatory endotype of the disease (Vărut et al., 2025).

In a Cochrane meta-analysis of 25 randomized clinical trials, omalizumab was shown to reduce asthma exacerbations by approximately 25% and reduce the need for ICS, but this benefit was most pronounced in patients with documented allergen sensitization and total IgE levels within a specific range (30–700 IU/mL in the adult population in the United States) (Vărut et al., 2025). In contrast, the anti-IL-5/IL-5Rα class showed a large reduction in exacerbations, providing a 53% reduction in the MENSA trial, while benralizumab provided a 51% reduction in the SIROCCO and CALIMA trials, but this benefit was specifically limited to patients with a certain blood eosinophil threshold (≥150–300 cells/μL), making this class less beneficial in the approximately 30–50% of the severe asthma population classified as type 2-low (Vărut et al., 2025). Dupilumab, which blocks the IL-4 and IL-13 co-receptor, showed greatest efficacy in patients with elevated eosinophils or FeNO, with much smaller benefits in the type 2-low subgroup (Mansour et al., 2026).

This variability in response is also evident at the cellular mechanism level: data from the MEX study showed that although mepolizumab significantly reduced blood eosinophils, approximately half of breakthrough exacerbations that still occurred during therapy were driven by residual eosinophilic inflammation, while the other half were non-eosinophilic (Vărut et al., 2025). Another study in patients receiving benralizumab found that approximately 27% of patients experienced a suboptimal response, which correlated with neutrophil-rich sputum and a history of previous viral or bacterial infections, suggesting a mixed endotype not fully addressed by a single drug mechanism of action (Vărut et al., 2025). These findings strengthen the argument that the effectiveness of biologic therapies is not solely a function of the drug's pharmacological potency, but also the result of an interaction between the drug's mechanism of action and each patient's specific inflammatory endotype, such that a drug that is highly effective in one subpopulation may provide minimal benefit in another.



Tezepelumab: Bridging Phenotypic Variability through Upstream Alarmin Blockade

The limitations of earlier biologics, which were only effective in the type 2-high phenotype, led to the development of tezepelumab, the first human monoclonal antibody targeting thymic stromal lymphopoietin (TSLP), an epithelial alarmin cytokine that acts as an upstream orchestrator of both type 2 and non-type 2 inflammatory pathways (Mansour et al., 2026). Because of its position at the apex of the inflammatory cascade, TSLP blockade has a broader effect than blockade of a single downstream cytokine such as IL-5 or IL-4/13 (Mansour et al., 2026).

In the phase 2b PATHWAY trial, tezepelumab 210 mg every 4 weeks reduced the annual exacerbation rate by 71% compared to placebo, and surprisingly, this benefit was consistent across the entire range of baseline blood eosinophil levels, including in patients with eosinophils below 150 cells/µL who were previously ineligible for anti-IL-5 therapy (Mansour et al., 2026). These results were replicated in the phase 3 NAVIGATOR trial with 1,061 patients, in which tezepelumab reduced the annual exacerbation rate by 56% and improved pre-bronchodilator FEV1 by 0.13 liters compared to placebo, with consistent benefit in the low-eosinophil subgroup (Mansour et al., 2026). In the SOURCE trial assessing the steroid-sparing effect in patients dependent on oral corticosteroids, significant benefit was only seen in the subgroup with blood eosinophils ≥150 cells/µL, indicating that although tezepelumab acts across phenotypes, the magnitude of benefit remains variable and is generally greater in patients with a higher burden of type 2 inflammation (Mansour et al., 2026).

The CASCADE mechanistic study also demonstrated that tezepelumab significantly reduced submucosal airway eosinophil counts across all biomarker subgroups, with improvements in mucus scores on CT imaging correlating with lung function improvement, indicating potential disease-modifying effects beyond symptom control (Mansour et al., 2026). Real-world data from the PASSAGE study in the United States also confirmed the effectiveness of tezepelumab in more diverse populations underrepresented in pivotal clinical trials, including Black patients, adolescents, smokers, and patients with mild-moderate COPD overlap, with annual exacerbation reductions ranging from 51% to 76%

(Mansour et al., 2026). However, a network meta-analysis showed that tezepelumab was not consistently statistically superior to other biologics in the pure type 2-high subgroup, so claims of superiority across phenotypes need to be interpreted proportionately: tezepelumab expands therapeutic coverage to the type 2-low population that previously lacked biologic options, but does not necessarily imply absolute superiority in all patient subgroups (Mansour et al., 2026).

Biomarkers as a Link between Drug Variability and Clinical Improvement

A consistent pattern emerging across the three therapy categories (conventional pharmacotherapy, AIT, and biologics) is that variability in drug effectiveness is closely related to the ability of biomarkers to predict individual response. A review of predictive biomarkers for asthma treatment confirmed that blood and sputum eosinophils, total IgE, and FeNO remain the most widely used conventional biomarkers to guide biologic therapy selection, although they provide only partial discrimination between type 2 subtypes and lack valid biomarkers for non-type 2 phenotypes (Bonnesen et al., 2023). In patients with exacerbations taking moderate-dose ICS, exacerbations correlated with lower blood and sputum eosinophils and higher sputum neutrophils, confirming that the inflammatory cell profile may guide the appropriateness of ICS therapy itself, not just biologics (Bonnesen et al., 2023).

The concept of precision medicine, or the treat-to-target approach, is increasingly recognized as a bridge between drug variability and consistent clinical improvement. Rather than a "treat-to-failure" strategy where standard therapy is administered uniformly and only adjusted after a patient experiences persistent loss of disease control, a precision approach integrates biomarkers and endotyping early in the disease course, with the goal of ensuring the right patient receives the right therapy at the right time while avoiding unnecessary exposure to less effective therapies (Bonnesen et al., 2023). This approach aligns with findings that the combination of AIT and biologics, or the selection of biologics based on personalized eosinophil/FeNO thresholds, consistently results in greater clinical improvement than the uniform administration of a single therapy across the asthma population (Batard et al., 2025).

Synthesis: Three-Dimensional Relationship - Effectiveness, Variability, and Clinical Improvement

Based on the above synthesis, it can be concluded that the relationship between drug effectiveness and clinical improvement in bronchial asthma is not a simple linear one, but is mediated by variability at three levels:

(1) the variability of the drugs themselves, including differences in molecular targets (from broad, non-specific ICS to highly specific biologics targeting a single upstream cytokine or alarmin);
(2) patient variability, including inflammatory endotype, baseline biomarker levels, and allergic comorbidities; and
(3) behavioral variability, including compliance and drug use techniques.

Drugs with mechanisms of action more upstream in the inflammatory cascade, such as tezepelumab, which targets TSLP, tend to show more consistent efficacy across phenotypes than drugs targeting a single downstream mediator such as IL-5, but still show a gradient in the magnitude of benefit that aligns with the patient's type 2 inflammatory burden (Vărut et al., 2025). Meanwhile, AIT demonstrates that the effectiveness of a therapeutic modality is also highly dependent on technical parameters of administration such as dose and duration, beyond patient biologic factors (Batard et al., 2025). In conventional pharmacotherapy, variability in clinical improvement can occur without any change in drug type at all, simply due to fluctuations in adherence over time in the same individual (Rackow et al., 2025).

CONCLUSION

The effectiveness of bronchial asthma medications and the clinical improvement achieved by patients are inextricably linked to variability at various levels: the type and target mechanism of action of the drug, the patient's endotype and inflammatory biomarkers, the dose and duration of therapy, and adherence to medication in practice. Conventional ICS-based pharmacotherapy remains the cornerstone of treatment, but its effectiveness is heavily influenced by patient adherence, which is often much lower

than self-reported. Allergen immunotherapy offers unique disease-modifying benefits, but the magnitude depends on the dose and duration of therapy.

Early-generation biologic therapies (anti-IgE, anti-IL-5/IL-5Rα, anti-IL-4Rα) provided a significant reduction in exacerbations but were limited to the type 2-high phenotype, while tezepelumab as a TSLP inhibitor extended the benefit across phenotypes to include type 2-low, although still showed variation in the magnitude of the effect according to the patient's type 2 biomarker burden. The clinical implication of these findings is the need for a personalized approach to biomarker-based therapy and continuous adherence assessment, rather than relying on a single pharmacological strategy, so that clinical improvement in bronchial asthma can be achieved optimally and sustainably across the entire spectrum of patient phenotypes.

BIBLIOGRAPHY

Batard T,et.al. *Allergen Immunotherapy for the Prevention and Treatment of Asthma*. Clin. Exp. Allergy. 2025;55:111–141.

Vărut RM,et.al. *Targeted Biologic Therapies in Severe Asthma: Mechanisms, Biomarkers, and Clinical Applications*. Pharma. 2025;18:1021.

Mansour GK, Kumar S, Sukkarieh HH. *Tezepelumab: redefining TSLP blockade in severe asthma through mechanistic precision and translational pharmacology*. Front. Pharmacol. 2026;17:1732906.

Jensen FF, Håkansson KEJ, Nielsen BO, Weinreich UM, Ulrik CS. *Self-reported vs. objectively assessed adherence to inhaled corticosteroids in asthma.* Asthma Res. Pract. 2021;7:5.

Rackow P, Drennan A, Pinnock H, Dima AL. *Optimizing adherence to medication to improve outcomes in asthma*. Curr. Opin. Pulm. Med. 2025;31(3):262–269.

Bonnesen B, Jensen JUS, Mathioudakis AG, Corlateanu A, Sivapalan P. *Promising treatment biomarkers in asthma.* Front. Drug Saf. Regul . 2023;3:1291471.

Global Initiative for Asthma.GINA. 2024.