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Biologic Therapies in Severe Pediatric Asthma: Mechanisms, Clinical Efficacy, and Precision Medicine Approaches

Special Issue: Update on Biologic Therapy in Pediatric Allergy

Carolina Grella[1], Cristiana Indolfi[1], Angela Klain[1], Alessandra Perrotta[1], Fabio Decimo[1], Giulio Dinardo[1], Michele Miraglia del Giudice[1]

[1] Department of Woman, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli," Naples, Italy; These authors contributed equally to this work

ABSTRACT

Severe asthma in children is a chronic and heterogeneous condition that is unresponsive to high-dose inhaled corticosteroids and long-acting beta2-agonists (LABAs), and is associated with significant morbidity, frequent use of systemic corticosteroids, and reduced quality of life. The advent of biologic therapies has transformed the management of severe asthma by targeting specific immunological pathways. This review examines the mechanisms of action, clinical efficacy, and safety of mepolizumab (anti-IL-5) and dupilumab (anti-IL-4Rα), approved for children aged ≥ 6 years, omalizumab (anti-IgE), the first biologic approved for asthma, and tezepelumab (anti-TSLP), recently authorized from age 12 also for patients with non-T2-high phenotypes. The analysis is based on a structured review of the literature in the PubMed database, including articles published between 2010 and 2025 and selected for their relevance to the management of severe pediatric asthma, the efficacy of biologic treatments, and clinical outcomes. Accurate identification of asthma phenotypes and endotypes – guided by biomarkers such as eosinophils, IgE, and FeNO measurement – is essential to personalize therapy and avoid ineffective treatments. Biologics provide proven benefits in reducing exacerbations, improving lung function and quality of life, and managing associated comorbidities. A thorough clinical and immunological evaluation remains essential to implement a precision medicine approach in the care of pediatric patients with severe asthma.

KEY WORDS: severe asthma; children; biologic therapy

INTRODUCTION

The advent of biologic drugs has revolutionized the management of severe asthma in pediatric patients. This therapy is based on the administration of monoclonal antibodies directed against key mediators of the T2-high and T2-low inflammatory responses underlying the disease. Type 2 inflammation is characterized by eosinophilic infiltration of the airways, increased fractional exhaled nitric oxide (FeNO), and up-regulation of cytokines such as IL-4, IL-5, and IL-13 [1-4]. Currently approved biologic drugs for pediatric use include omalizumab (anti-IgE), mepolizumab (anti-IL-5), benralizumab (anti-IL-5Rα), and dupilumab (anti-IL-4Rα). More recently, tezepelumab (anti-TSLP) has been authorized for use in adolescents [5]. The aim of this review is to provide an updated summary of the available evidence on these drugs for severe pediatric asthma, analyzing their mechanisms of action, clinical trial data, safety profile, and patient selection criteria.

The decision to initiate biologic therapy in children with asthma requires a careful and precise evaluation of both the phenotype and endotype of the disease, together with an assessment of

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CORRESPONDENCE

Alessandra Perrotta
alessandraperrotta96@gmail.com

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specific biomarkers that may help predict treatment response. Asthma phenotypes refer to the observable clinical characteristics presented by the patient. In the pediatric population, the most common phenotype is allergic eosinophilic asthma, often associated with other atopic conditions such as eczema and allergic rhinitis [6]. Other phenotypes include late-onset asthma or obesity-related asthma, but these are less frequently observed in children. Endotypes, on the other hand, reflect the underlying molecular and immunological mechanisms driving the disease. Among these, the T2-high endotype is the best characterized in asthma. It is driven by both adaptive (Th2) and innate (ILC2) immune responses, leading to the production of key cytokines such as IL-4, IL-5, and IL-13, which recruit eosinophils into the airways, increase IgE synthesis, and contribute to mucus hypersecretion – all central features of the pathophysiology of type 2-high asthma [7].

In clinical practice, several biomarkers are used to help identify these phenotypes and endotypes and to guide biologic therapy. Blood eosinophil count is one of the most widely used; a baseline count of ≥ 150/μL, or ≥ 300/μL in the previous year, is generally associated with a favorable response to anti-IL-5 and anti-IL-4/13 therapies [8]. Fractional exhaled nitric oxide (FeNO) is another useful biomarker: levels ≥ 20 ppb suggest the presence of T2 airway inflammation and can help predict response to inhaled corticosteroids as well as biologic treatments [9]. Finally, measurement of serum total IgE and allergen-specific IgE supports the diagnosis of allergic asthma and is essential when considering eligibility for anti-IgE therapy. Importantly, these biomarkers should never be interpreted in isolation. Clinical features, prior treatment history, frequency of exacerbations, and the presence of comorbidities must all be taken into account. Careful phenotyping and endotyping enable clinicians to select the biologic agent most likely to benefit each individual patient, optimizing outcomes and avoiding unnecessary exposure to ineffective therapies (Tab. I).

MEPOLIZUMAB

Mepolizumab is a humanized monoclonal antibody (IgG1) that specifically targets interleukin-5 (IL-5), a cytokine crucial for the maturation, activation, and survival of eosinophils. By binding to IL-5, the drug inhibits its interaction with its receptor on eosinophils, thereby reducing their proliferation and survival both in peripheral blood and airway tissues. This mechanism results in a significant reduction of eosinophilic inflammation and, consequently, in asthma exacerbations associated with this inflammatory profile [10]. In Europe, both the EMA and AIFA have approved mepolizumab for pediatric use from the age of 6 years in children with severe eosinophilic asthma that remains uncontrolled despite high-dose inhaled corticosteroids combined with long-acting beta2-agonists (ICS/LABA). Eligibility for treatment requires documented peripheral eosinophilia and a history of frequent asthma exacerbations, which are characteristic of the T2-high inflammatory phenotype. Benralizumab, on the other hand, acts by directly binding to the interleukin-5 receptor (IL-5Rα), leading to eosinophil depletion through a cytotoxic mechanism mediated by effector cells. The drug is approved for the treatment of severe eosinophilic asthma in adults and pediatric patients from 12 years of age, as its efficacy and safety in younger children are still under investigation [11]. The efficacy of mepolizumab has been demonstrated in pivotal trials such as DREAM and MENSA, which reported up to a 50% reduction in annual exacerbation rates, improvements in lung function (measured by FEV1), and reduced dependence on oral corticosteroids (OCS) in adult populations [12,13]. Pediatric data, although more limited, are encouraging. Extension studies and real-world analyses suggest similar benefits in adolescents, while further support comes from studies in children aged 6 to 11 years. These studies have demonstrated significant reductions in exacerbation frequency and meaningful improvements in quality of life metrics [14]. Pharmacokinetic analyses tailored for the pediatric population have confirmed that systemic drug exposure in children, when dosed

TABLE I. Overview of currently approved biologic therapies for severe pediatric asthma, showing their molecular targets, mechanisms of action, and key biomarkers for guiding patient selection. This table highlights the rationale for selecting specific biologics based on disease phenotype and endotype.

Drug	Target	Mechanism of action	Key biomarkers for eligibility
Omalizumab	IgE	Binds circulating IgE, preventing its interaction with FcεRI on mast cells and basophils	Total serum IgE within dosing range; allergen-specific IgE; allergic phenotype
Mepolizumab	IL-5	Blocks IL-5, reducing eosinophil maturation, survival, and recruitment	Blood eosinophils ≥ 150/μL (or ≥ 300/μL in previous year); T2-high inflammation
Benralizumab	IL-5Rα	Induces apoptosis of eosinophils and basophils via antibody-dependent cell-mediated cytotoxicity (ADCC)	Blood eosinophils ≥ 150/μL; history of frequent exacerbations
Dupilumab	IL-4Rα	Inhibits IL-4 and IL-13 signaling, reducing type 2 inflammation and IgE synthesis	Elevated eosinophils and/or FeNO ≥ 20 ppb; comorbid atopic diseases
Tezepelumab	TSLP	Blocks epithelial alarmin TSLP, upstream regulator of multiple inflammatory pathways	No biomarker restriction (effective across T2-high and some T2-low phenotypes)

according to body weight, is comparable to that observed in adults. This finding supports the current dosing strategy, which recommends 40 mg subcutaneously every four weeks in children aged 6 to 11 years, and 100 mg in individuals aged 12 years and older [11,15]. In real-world pediatric cohorts, initiation of mepolizumab therapy has been associated with a substantial decrease in hospitalizations and reduced reliance on systemic corticosteroids within 6 months of treatment initiation [14]. Regarding safety, mepolizumab has shown a reassuring profile. Most adverse events are mild and transient, such as headache, nasopharyngitis, and injection-site reactions. Rare but relevant complications include hypersensitivity reactions and herpes zoster reactivation. Importantly, long-term follow-up studies have not shown an increased risk of serious infections or malignancies [16].

OMALIZUMAB

Omalizumab is a humanized monoclonal antibody that selectively binds to circulating free IgE, preventing its interaction with high-affinity receptors (FcεRI) on mast cells and basophils. This action reduces the activation and release of pro-inflammatory mediators, thereby modulating the allergic response underlying type 2 asthma [33]. Its efficacy has been demonstrated in patients with moderate-to-severe allergic asthma inadequately controlled by optimized inhaled therapy: omalizumab improves lung function, reduces exacerbations, and enhances quality of life [34,36]. The rationale for its use is based on the central role of IgE in the pathogenesis of allergic asthma: IgE promotes mast cell degranulation and the activation of eosinophils and other effector cells, sustaining chronic airway inflammation. Omalizumab reduces not only free IgE but also the expression of FcεRI receptors on effector cells, resulting in a cascade effect that diminishes allergic sensitization [37]. Randomized clinical trials and meta-analyses have documented a significant reduction in exacerbations and improved respiratory function in treated patients, with clinical benefits tending to be more pronounced in patients with higher serum IgE levels and sensitization to multiple aeroallergens [38,39]. However, it is important to note that, unlike drugs such as tezepelumab, the prescription of omalizumab is limited to documented IgE-mediated allergy and specific ranges of total plasma IgE, making it indicated only for a subgroup of patients with type 2 asthma [38,40]. The drug has also been extensively studied in pediatric and adolescent populations, showing a favorable safety and efficacy profile, with improvements in clinical control and reduced exacerbations [34]. Furthermore, cost-effectiveness analyses conducted in various healthcare settings have suggested that omalizumab represents a sustainable option in healthcare systems where it has been introduced, particularly for patients with frequent exacerbations and hospitalizations [35]. The safety profile of omalizumab is generally favorable: the most common adverse events are injection site reactions, headache, and arthralgia; anaphylactic reactions are rare but possible and require monitoring during initial administrations [38]. In summary, omalizumab represents the first biologic approved for severe asthma and remains a cornerstone of treatment in patients with allergic phenotypes and IgE-mediated sensitization, although new therapies targeting upstream inflammatory pathways now offer a broader range of therapeutic options [40].

DUPILUMAB

Dupilumab is a humanized IgG4 monoclonal antibody that exerts its therapeutic effects by binding to the alpha subunit of the interleukin-4 receptor (IL-4Rα). This action blocks the signaling pathway shared by IL-4 and IL-13, two cytokines involved in the type 2 inflammatory cascade. Inhibition of this pathway results in broad immunomodulatory effects, including, for example, a reduction in IgE synthesis and decreased recruitment of eosinophils into the airways. Overall, these actions lead to a marked attenuation of Th2-mediated inflammation. This biologic drug is approved from the age of 6 years for severe refractory asthma characterized by a Th2-high inflammatory profile. Dupilumab is administered subcutaneously every two weeks, with dosage adjusted according to body weight, in accordance with EMA and FDA guidelines [40,41]. The efficacy of dupilumab in pediatric asthma has been demonstrated in several phase III trials. The QUEST and VENTURE studies showed marked reductions in the rate of severe exacerbations – up to 70% in some subgroups – as well as significant improvements in pre-bronchodilator FEV1 and notable corticosteroid-sparing effects [19,20]. Pediatric subgroup analyses from these studies have demonstrated consistent benefits in adolescents. Further confirmation comes from the VOYAGE study, conducted specifically in children aged 6 to 11 years, which reported substantial reductions in annualized exacerbation rates, improvements in asthma control scores, and better quality of life outcomes [21]. Beyond its primary respiratory benefits, dupilumab has shown a broader impact on systemic markers of type 2 inflammation: it significantly reduces FeNO levels, circulating eosinophils, and serum IgE, indicating robust suppression of the immunologic mechanisms underlying severe asthma. Moreover, dupilumab has proven effective in patients with comorbidities such as allergic rhinitis, atopic dermatitis, and eosinophilic esophagitis, which often coexist with asthma and worsen patients' quality of life [22]. From a safety standpoint, dupilumab has a very favorable tolerability profile. The most common adverse effects include injection-site reactions, mild transient increases in blood eosinophils, and conjunctivitis. More serious events, such as eosinophilic pneumonia and vasculitis, are rare but should be monitored in clinical practice, especially in at-risk individuals. It is important to note that dupilumab does not increase the risk of anaphylaxis or cause systemic immunosuppression, making it a safe long-term treatment option for many pediatric patients [20,23].

TEZEPELUMAB

Tezepelumab is a humanized monoclonal antibody that binds to and neutralizes thymic stromal lymphopoietin (TSLP), preventing its interaction with the heterodimeric receptor and thereby blocking upstream activation of the inflammatory cascade characteristic of

severe asthma [28]. TSLP is produced by airway epithelial cells in response to environmental stimuli such as allergens, viruses, pollutants, and smoke, and plays a crucial role in triggering inflammation by promoting dendritic cell activation, Th2 lymphocyte differentiation, and expansion of type 2 innate lymphoid cells (ILC2), as well as modulating eosinophil and mast cell activity [32]. The results of the PATHWAY and NAVIGATOR clinical trials have shown that treatment with tezepelumab significantly reduces the annualized rate of exacerbations (up to 56% compared with placebo) and improves lung function, with benefits also observed in patients with low eosinophil counts or FeNO. This is particularly relevant because it differentiates tezepelumab from other currently available biologics, as its prescription does not require evidence of elevated blood eosinophils or other type 2 inflammation biomarkers [24,27]. Network meta-analyses have further suggested that tezepelumab has comparable or even superior efficacy to mepolizumab, benralizumab, and dupilumab in patients with eosinophilic asthma [25].

In clinical practice, the indications for tezepelumab include patients with severe uncontrolled asthma despite high-dose inhaled therapy based on corticosteroids and long-acting bronchodilators. Real-world studies conducted in Germany and Spain have confirmed the efficacy observed in trials, reporting reductions in exacerbations and improvements in quality of life even in routine clinical practice [29,31]. Regarding contraindications, these include hypersensitivity to the active substance or excipients, while data on safety and efficacy in pregnancy, lactation, and younger pediatric populations remain limited, although good tolerability has already been reported in adolescents [30]. The drug's safety profile is generally favorable: in registration studies, the most common adverse events were mild to moderate, such as nasopharyngitis, headache, and local injection site reactions, with incidence similar to placebo; systemic hypersensitivity reactions were rare [27,28]. No new or unexpected toxicity signals have emerged to date, but long-term monitoring is recommended, particularly to evaluate safety in special populations and prolonged treatments. In summary, tezepelumab represents one of the most innovative biologic therapies for severe asthma, acting "upstream" by blocking TSLP and interfering with both eosinophilic and non-eosinophilic inflammatory mechanisms. This makes it particularly relevant in patients with phenotypes that are less responsive to other currently available biologics, significantly expanding the therapeutic arsenal against refractory severe asthma [24,27].

DISCUSSION

Severe asthma in children is a multifaceted and heterogeneous disease, imposing substantial burden on both patients and healthcare systems [46,47]. Despite high-dose inhaled corticosteroids and long-acting beta2-agonists, many children continue to experience persistent symptoms and frequent exacerbations, often necessitating oral corticosteroids with their associated long-term adverse effects [3]. The advent of biologic therapies has dramatically reshaped the management landscape, offering targeted treatment options that directly interfere with the underlying immunological mechanisms of type 2 (T2) inflammation [4,5]. Accurate characterization of pediatric asthma through phenotyping and endotyping is critical to ensure the optimal use of these therapies. Allergic eosinophilic asthma remains the most common phenotype in children, which is frequently associated with comorbid atopic conditions such as eczema and allergic rhinitis [6]. Underpinning this phenotype, T2-high endotypes are characterized by elevated levels of IL-4, IL-5, and IL-13, eosinophilic airway inflammation, and increased IgE production [7]. Biomarkers including blood eosinophil count, FeNO, and serum IgE help to guide treatment decisions and predict response, but must always be interpreted alongside clinical features, exacerbation history, and comorbidities [8,9]. Biologics now allow a precision medicine approach, reducing exacerbations, improving lung function, and minimizing corticosteroid exposure. Their use in children has been increasingly supported by clinical trials, extension studies, and real-world data [14,21,31]. For example, therapies targeting the IL-5 or IL-5Rα pathways effectively decrease eosinophilic inflammation, while agents blocking IL-4/IL-13 signaling or IgE modulate broader allergic and T2 inflammatory cascades. More recent interventions, such as TSLP inhibition, act upstream in the inflammatory pathway, offering benefits even in children with low eosinophil counts or mixed phenotypes [24,27]. The integration of biologics into pediatric practice has demonstrated consistent improvements not only in asthma control, but also in quality of life and reduction of healthcare resource utilization [14,34,45]. Moreover, several studies have highlighted the additional benefit of some agents in managing comorbid atopic conditions, addressing the complex interplay of T2 inflammation beyond the airways [22,42]. Safety profiles across agents are generally favorable, with most adverse events being mild or transient, although careful monitoring remains important, especially during initiation and in children with higher risk of hypersensitivity reactions [16,23,38]. Importantly, the growing evidence base emphasizes that biologic therapies are not interchangeable and that selection should be individualized. Decisions should incorporate biomarker levels, phenotypic characteristics, comorbidities, prior response to therapies, and patient-specific considerations. Real-world data have reinforced trial findings, demonstrating that consistent adherence and early initiation of biologics in eligible patients can substantially reduce exacerbations, hospitalizations, and corticosteroid dependence, translating into both clinical and economic benefits [29,31,44,45]. As biologic options expand, clinicians are better equipped to tailor therapy to each child's unique immunological profile, moving toward a more nuanced and effective management of severe asthma [40,46,47].

CONCLUSIONS

The emergence of biologic therapies represents a transformative advance in the treatment of pediatric severe asthma. By precisely targeting the immunopathologic drivers of inflammation, these agents provide meaningful improvements in symptom control, lung function, and quality of life while mitigating the risks associated with systemic

corticosteroid use. An important aspect is the possibility of gradually reducing the dose of inhaled corticosteroids in patients who respond positively to biologic therapy, an approach that not only lowers the risk of side effects associated with long-term corticosteroid use but also helps improve treatment adherence and the patient's quality of life. Optimal management relies on careful phenotyping, endotyping, and biomarker evaluation to match patients with the therapy most likely to confer benefit. Real-world and trial evidence consistently support the safety, efficacy, and cost-effectiveness of these treatments in children, highlighting their central role in modern precision medicine approaches. As research continues to refine indications and explore new mechanisms, the expanding therapeutic arsenal promises better outcomes for children with severe asthma, particularly for those who are previously unresponsive to conventional therapies [30,40-47].

Ethical consideration

As this study is based on publicly available online datasets, ethical approval and informed consent are not applicable.

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Conflicts of interest statement

The authors declare no conflicts of interest.

Author's contributions

Conceptualization, C.G.; C.I; methodology, C.G; A.P.; writing-original draft preparation, C.G.; C.I.; A.K.; A.P.; G.D.; writing-review and editing, C.I.; supervision, M.MdG;

References

1 Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2023.

2 Dinardo G. Studio multicentrico comparativo sull'utilizzo di farmaci biologici nel trattamento dell'asma allergica grave in età pediatrica. Tesi di Laurea in Pediatria, Università della Campania "L. Vanvitelli" 2023.

3 Nunes C, Pereira AM, Morais-Almeida M. Asthma costs and social impact. Asthma Res Pract 2017;3:1. https://doi.org/10.1186/s40733-016-0029-3

4 Agache I, Song Y, Posso M, et al. Biologicals in severe asthma: a systematic review and network meta-analysis. Allergy 2021;76:3654-3671.

5 Menzies-Gow A, Corren J, Bourdin A, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med 2021;384:1800-1809. https://doi.org/10.1056/NEJMoa2034975.

6 Belgrave DC, Simpson A, Custovic A. Challenges in interpreting wheeze phenotypes: the clinical utility of phenotyping. Curr Opin Allergy Clin Immunol 2014;14:27-34.

7 Lambrecht BN, Hammad H. The immunology of asthma. Nat Immunol 2015;16:45-56. https://doi.org/10.1038/ni.3049

8 Pavord ID, Beasley R, Agusti A, et al. After asthma: redefining airways diseases. Lancet 2018;391:350-400. https://doi.org/10.1016/S0140-6736(17)30879-6

9 Malinovschi A, Fonseca JA, Jacinto T, et al. FeNO as a biomarker of asthma control. Allergy 2021;76:1147-1158.

10 Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014;371:1198-1207. https://doi.org/10.1056/NEJMoa1403290.

11 EMA. Nucala (mepolizumab). Summary of Product Characteristics. 2023.

12 Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med 2014;371:1189-1197. https://doi.org/10.1056/NEJMoa1403291

13 Ortega HG, et al. Mepolizumab efficacy in the MENSA trial. N Engl J Med 2014;371:1198-1207.

14 Gupta A, Ikeda M, Geng B, et al. Long-term safety and efficacy of mepolizumab in children with severe eosinophilic asthma. J Allergy Clin Immunol Pract 2020;8:1342-1351.e5.

15 Mukherjee M, Aleman Paramo F, Kjarsgaard M, et al. Weight-adjusted intravenous mepolizumab in severe asthma. Eur Respir J 2018;51:1702420.

16 EMA. Nucala SPC. 2023.

17 Gandhi NA, Bennett BL, Graham NM, et al. Targeting key proximal drivers of type 2 inflammation in disease. Nat Rev Drug Discov 2016;15:35-50. https://doi.org/10.1038/nrd4624

18 EMA. Dupixent (dupilumab): Summary of Product Characteristics. 2023.

19 Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med 2018;378:2486-2496. https://doi.org/10.1056/NEJMoa1804092

20 Wenzel S, Ford L, Pearlman D, et al. Dupilumab in persistent asthma with elevated eosinophil levels. N Engl J Med 2013;368:2455-2466. https://doi.org/10.1056/NEJMoa1304048

21 Bacharier LB, Maspero JF, Katelaris CH, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. N Engl J Med 2021;385:2230-2240. https://doi.org/10.1056/NEJMoa2106567.

22 Wenzel SE, et al. Integrated control of T2 comorbidities with dupilumab. J Allergy Clin Immunol 2019;143:682-689.

23 Dupixent long-term safety data. EMA Reports. 2023.

24 Caminati M, Buhl R, Corren J, et al. Tezepelumab in patients with allergic and eosinophilic asthma. Allergy 2024;79:1134-1145. https://doi.org/10.1111/all.15986.

25 Nopsopon T, Lassiter G, Chen ML, et al. Comparative efficacy of tezepelumab to mepolizumab, benralizumab, and dupilumab in eosinophilic asthma: A Bayesian network meta-analysis. J Allergy Clin Immunol 2023;151:747-755. https://doi.org/10.1016/j.jaci.2022.11.021.

26 Corren J, Menzies-Gow A, Chupp G, et al. Efficacy of Tezepelumab in Severe, Uncontrolled Asthma: Pooled Analysis of the PATHWAY and NAVIGATOR Clinical Trials. Am J Respir Crit Care Med 2023;208:13-24. https://doi.org/10.1164/rccm.202210-2005OC.

27 Kurihara M, Kabata H, Irie M, et al. Current summary of clinical studies on anti-TSLP antibody, Tezepelumab, in asthma. Allergol Int 2023;72:24-30. https://doi.org/10.1016/j.alit.2022.11.006.

28 Biener L, Mümmler C, Hinze CA, et al. Real-World Data on Tezepelumab in Patients with Severe Asthma in Germany. J Allergy Clin Immunol Pract 2024;12:2399-2407.e5. https://doi.org/10.1016/j.jaip.2024.05.052.

29 Bacharier LB, Jackson DJ. Biologics in the treatment of asthma in children and adolescents. J Allergy Clin Immunol 2023;151:581-589. https://doi.org/10.1016/j.jaci.2023.01.002.

30 Miralles-López JC, Bravo-Gutierrez FJ, Andújar-Espinosa R, et al.; RE-ASGRAMUR Group. Real-life effectiveness of tezepelumab in severe asthma. Allergol Immunopathol (Madr) 2025;53:163-173. https://doi.org/10.15586/aei.v53i2.1326.

31 Smolinska S, Antolín-Amérigo D, Popescu FD, et al. Thymic Stromal Lymphopoietin (TSLP), Its Isoforms and the Interplay with the Epithelium in Allergy and Asthma. Int J Mol Sci 2023;24:12725. https://doi.org/10.3390/ijms241612725.

32 Gauvreau GM, Hohlfeld JM, FitzGerald JM, et al. Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma. Eur Respir J 2023;61:2201193. https://doi.org/10.1183/13993003.01193-2022.

33 Cheng L, Yang T, Ma X, et al. Effectiveness and Safety Studies of Omalizumab in Children and Adolescents with Moderate-To-Severe Asthma. J Pharm Pract 2023;36:370-382. https://doi.org/10.1177/08971900211038251.

34 Buendía JA, Guerrero Patiño D, Zuluaga Salazar AF. Cost effectiveness of omalizumab for severe asthma in Colombia. J Asthma 2024;61:292-299. https://doi.org/10.1080/02770903.2023.2267129.

35 Liao J, Tang J, Jiang Y, et al. Effects of omalizumab on lung function in patients with moderate-to-severe allergic asthma: a systematic review and meta-analysis. Ther Adv Respir Dis 2024;18:17534666231221771. https://doi.org/10.1177/17534666231221771.

36 Tajiri T, Suzuki M, Kutsuna T, et al. Specific IgE Response and Omalizumab Responsiveness in Severe Allergic Asthma. J Asthma Allergy 2023;16:149-157. https://doi.org/10.2147/JAA.S393683.

37 Agache I, Beltran J, Akdis C, et al. Efficacy and safety of treatment with biologicals (benralizumab, dupilumab, mepolizumab, omalizumab and reslizumab) for severe eosinophilic asthma. A systematic review for the EAACI Guidelines - recommendations on the use of biologicals in severe asthma. Allergy 2020;75:1023-1042. https://doi.org/10.1111/all.14221.

38 Hanania NA, Alpan O, Hamilos DL, Condemi JJ, Reyes-Rivera I, Zhu J, Rosen KE, Eisner MD, Wong DA, Busse W. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. Ann Intern Med 2011;154:573-82. https://doi.org/10.7326/0003-4819-154-9-201105030-00002. Erratum in: Ann Intern Med 2019;171:528. https://doi.org/10.7326/L19-0549. P

39 Pelaia C, Melhorn J, Hinks TS, et al. Type 2 severe asthma: pathophysiology and treatment with biologics. Expert Rev Respir Med 2024;18:485-498. https://doi.org/10.1080/17476348.2024.2380072.

40 Bacharier LB, Maspero JF, Katelaris CH, et al.; Liberty Asthma VOYAGE Investigators. Dupilumab in Children with Uncontrolled Moderate-to-Severe Asthma. N Engl J Med 2021;385:2230-2240. https://doi.org/10.1056/NEJMoa2106567.

41 Pavord ID, Rabe KF, Israel E, et al. Dupilumab Induces Long-Term On-Treatment Clinical Remission in Patients with Type 2 Asthma. J Allergy Clin Immunol Pract 2025;13:132-142. https://doi.org/10.1016/j.jaip.2024.10.009.

42 Brusselle GG, Koppelman GH. Biologic Therapies for Severe Asthma. N Engl J Med 2022;386:157-171. https://doi.org/10.1056/NEJMra2032506.

43 Nopsopon T, Brown A, Hahn G, et al. Temporal variation in the effectiveness of biologics in asthma: Effect modification by changing patient characteristics. Respir Med 2024;234:107802. https://doi.org/10.1016/j.rmed.2024.107802.

44 Bird JA, Near AM, Wang J, et al. Health care resource utilization of patients with asthma and food allergy initiating omalizumab. J Allergy Clin Immunol Glob 2025;4:100491. https://doi.org/10.1016/j.jacig.2025.100491.

45 De Keyser HH, Anderson WC 3rd, Stempel DA, et al. Digital Health for Asthma Management: Electronic Medication Monitoring for Adherence as a Case Example. J Allergy Clin Immunol Pract 2025;13:1518-1526. https://doi.org/10.1016/j.jaip.2024.12.042.

46 Pelaia C, Crimi C, Vatrella A, Tinello C, Terracciano R, Pelaia G. Molecular Targets for Biological Therapies of Severe Asthma. Front Immunol 2020;11:603312. https://doi.org/10.3389/fimmu.2020.603312.

47 Indolfi C, Klain A, Capuano MC, et al. Severe Asthma in School-Age Children: An Updated Appraisal on Biological Options and Challenges in This Age Group. Children (Basel) 2025;12:167. https://doi.org/10.3390/children12020167.