

Exploring the Potential Benefits of Biologic Therapies Beyond Respiratory Allergy

Rossella Sica¹, Francesco Catamerò^{2,3}, Simone Foti Randazzese^{4,5}, Francesca Galletta⁶, Amelia Licari^{4,5}, Gian Luigi Marseglia^{4,5}, Francesca Mori³, Remo Poto⁷, Federica Pulvirenti⁸, Silvia Ricci^{2,9}, Mattia Giovannini^{2,3,*}, Sara Manti^{6,*}

¹Department of Pediatrics, "San Luca" Hospital, Vallo della Lucania, ASL Salerno, Italy; ²Department of Health Sciences, University of Florence, Florence, Italy; ³Allergy Unit, Meyer Children's Hospital IRCCS, Florence, Italy; ⁴Pediatric Unit, Department of Clinical, Surgical, Diagnostic, and Pediatric Sciences, University of Pavia, Pavia, Italy; ⁵Pediatric Clinic, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; ⁶Pediatric Unit, Department of Human Pathology of Adult and Childhood Gaetano Barresi, University of Messina, Messina, Italy; ⁷Department of Translational Medical Sciences, University of Naples Federico II, Naples, Italy; ⁸Reference Centre for Primary Immune Deficiencies, Sapienza University Hospital Policlinico Umberto I, Rome, Italy; ⁹Immunology Unit, Meyer Children's Hospital IRCCS, Florence, Italy

*These authors contributed equally to this work

Correspondence: Francesco Catamerò, Department of Health Sciences, University of Florence, Viale Pieraccini 24, Florence, 50139, Italy, Email francesco.catamero@unifi.it

Abstract: Severe pediatric asthma is a heterogeneous inflammatory disease that is most commonly driven by type 2 (T2) inflammation. Because respiratory viral infections are the leading triggers of asthma exacerbations in children, this review examines the effects of biologic therapies on infection-related outcomes and antiviral immune function, beyond their established role in asthma control. We conducted a structured narrative review of literature published from January 2000 through February 2026 using PubMed/MEDLINE, EMBASE, Scopus, and the Cochrane Library databases. Studies evaluating infection-related outcomes and immune effects of biologic therapies in pediatric asthma were analyzed. Available evidence consistently indicates that biologics have favorable infectious safety profiles without increasing the risk of serious or opportunistic infections. Anti-IgE therapy (omalizumab) showed the strongest evidence of direct immunomodulatory effects, including restoration of interferon-mediated antiviral responses and reduction of virus-triggered asthma exacerbations. Anti-IL-5 and anti-IL-5 receptor therapies have corticosteroid-sparing effects and preserve immune competence despite eosinophil depletion. Dupilumab and tezepelumab similarly provide sustained efficacy and stable safety profiles without increasing infectious burden. Real-world evidence from the COVID-19 pandemic further indicates that biologic-treated children do not have greater susceptibility to SARS-CoV-2 infection or more severe disease. Overall, biologic therapies appear to provide targeted immunomodulation rather than broad immunosuppression, preserving host defense while controlling severe pediatric asthma. These findings suggest that biologic therapies may positively influence immune competence beyond asthma control, with implications for infection susceptibility and antiviral defense. Further prospective pediatric studies with standardized endpoints and long-term follow-up are needed to define their immunological impact and optimize precision-medicine strategies.

Keywords: biologic drugs, omalizumab, tezepelumab, dupilumab, benefits, asthma

Introduction

Severe pediatric asthma presents a major clinical and immunological challenge and accounts for a disproportionate burden of morbidity despite its relatively low prevalence. According to the Global Initiative for Asthma (GINA) 2025 report, severe asthma is defined as disease that remains uncontrolled despite optimized Step 4–5 therapy—including high-dose inhaled corticosteroids (ICS) combined with long-acting β_2 -agonists—or that worsens when treatment is reduced.¹ Asthma affects approximately 10–15% of children in industrialized countries.² Although only 5–10% meet the criteria for severe disease, this subgroup has the highest rates of exacerbations, hospitalizations, systemic corticosteroid exposure, and long-term complications.^{1,3–5}

Severe asthma is increasingly recognized as a heterogeneous, endotype-driven condition that is most commonly sustained by type 2 (T2) inflammation, characterized by immunoglobulin E (IgE), eosinophils, and T-helper 2 (Th2) cytokines, including interleukin (IL)-4, IL-5, and IL-13.^{4,6} Beyond airway inflammation and hyperresponsiveness, T2-driven disease is associated with epithelial barrier dysfunction and impaired innate immune signaling within the airway mucosa.⁷ The respiratory epithelium therefore serves as a key regulator of immune responses by coordinating antiviral defense and mucosal homeostasis.

Respiratory viral infections are the leading triggers of asthma exacerbations in childhood and account for most asthma-related hospitalizations.^{8–10} Rhinovirus, respiratory syncytial virus, and influenza virus are consistently implicated.^{8–10} Mechanistic studies indicate that children with allergic asthma exhibit impaired production of type I and III interferons by airway epithelial and plasmacytoid dendritic cells, resulting in defective antiviral responses.^{8,11} This deficiency promotes viral replication and amplifies airway inflammation, thereby increasing susceptibility to severe exacerbations.⁹ Consequently, infection-related morbidity reflects environmental exposure together with intrinsic dysregulation of immune–epithelial crosstalk within a T2-skewed milieu.^{7–11}

Historically, the management of severe pediatric asthma relied on escalating anti-inflammatory therapy, particularly systemic corticosteroids. Although effective, prolonged corticosteroid exposure is associated with clinically important adverse effects in children, including increased infection risk, impaired growth, metabolic complications, and psychological disturbances.¹² Inhaled corticosteroids may similarly exert dose-dependent systemic effects, including growth suppression.¹³ These limitations have driven the need for therapies that selectively target pathogenic pathways without inducing broad immunosuppression. Furthermore, the pediatric immune system differs substantially from that of adults, with an evolving balance between innate and adaptive immunity, ongoing thymus-dependent T-cell maturation, and distinct patterns of antiviral interferon signaling that may increase susceptibility to respiratory viral infections while enhancing responsiveness to immunomodulatory interventions.^{8,11} Nevertheless, pediatric-specific evidence on the immunological effects of biologic therapies remains considerably more limited than that in adults, underscoring the need to synthesize pediatric data rather than extrapolate from adult studies.

Biologic therapies have reshaped the treatment paradigm for severe pediatric asthma.^{14,15} These monoclonal antibodies selectively target key mediators of T2 inflammation and are recommended at Step 5 for children and adolescents with T2-driven disease after standard therapy has been optimized.¹ The European Academy of Allergy and Clinical Immunology (EAACI) similarly supports their use based on randomized trials and systematic reviews.^{16–19} Currently available agents include anti-IgE (omalizumab), anti-IL-5 and anti-IL-5 receptor (mepolizumab and benralizumab), anti-IL-4 receptor α (dupilumab), and upstream inhibitors targeting epithelial alarmins such as thymic stromal lymphopoietin (tezepelumab).^{1,16–18} These therapies consistently reduce exacerbations and systemic corticosteroid use, with favorable safety profiles and no evidence of clinically relevant global immunosuppression.^{1,16–18,20}

Beyond asthma control, increasing attention has focused on the broader immunological effects of biologics, particularly infection susceptibility and antiviral immunity. Despite initial concerns, evidence from clinical trials, observational studies, and guideline-based analyses does not indicate an increased risk of serious or opportunistic infections among patients receiving biologics.^{16–18,20} This evidence supports the distinction between immunomodulation and immunosuppression: biologics selectively target defined pathways while preserving overall immune competence.

Emerging evidence suggests that biologics may enhance host defense mechanisms. Anti-IgE therapy increases interferon- α production and antiviral responses in allergic asthma.^{21–23} Anti-IL-5/IL-5R and anti-IL-4R α therapies may indirectly reduce infection-related morbidity through corticosteroid-sparing effects and improved airway stability.^{24–28} Tezepelumab has demonstrated significant reductions in exacerbations without increasing infectious risk.²⁹ Real-world evidence from the COVID-19 pandemic further supports infectious safety, indicating no increased susceptibility to SARS-CoV-2 infection or disease severity among children receiving biologics.^{30–32}

Collectively, these findings suggest that biologic therapies may influence immune competence beyond asthma control, with implications for infection susceptibility and antiviral defense. However, previous reviews of biologics in pediatric asthma have largely focused on exacerbation reduction and lung function, with comparatively limited attention to infection-related outcomes. This review therefore synthesizes current evidence on the broader immunological effects

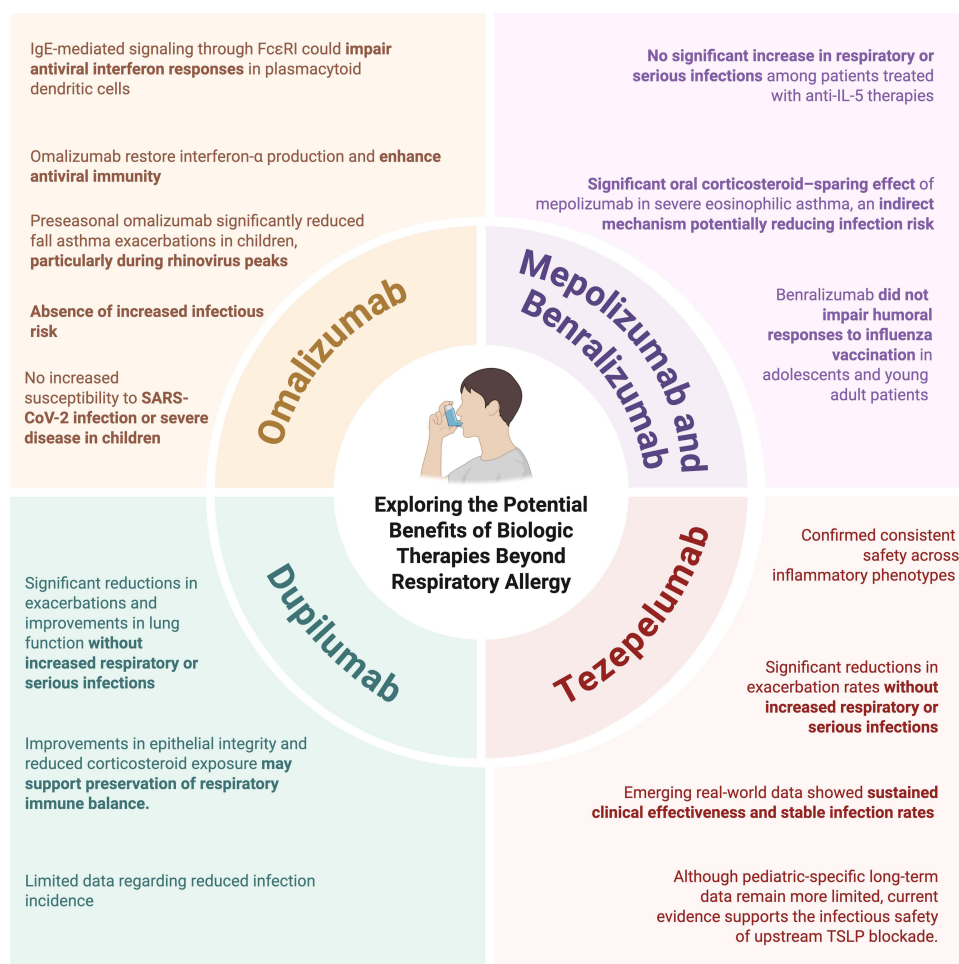


Figure 1 Summary of the reported benefits of biologic therapies beyond asthma. Created with Biorender.com.

of biologic therapies in severe pediatric asthma, focusing on infection-related outcomes, antiviral immune responses, and infectious safety across biologic classes (Figure 1).

Methodology

A structured search of PubMed/MEDLINE, EMBASE, Scopus, and the Cochrane Library was conducted for literature published from January 2000 through February 2026. The search used the following terms: “asthma,” “children,” “adolescents,” “biologic therapy,” “omalizumab,” “mepolizumab,” “benralizumab,” “dupilumab,” “tezepelumab,” “infection,” “respiratory infection,” “viral exacerbation,” “antiviral immunity,” and “corticosteroid-sparing.” Studies evaluating infection-related or immune outcomes of biologic therapies in pediatric asthma were selected according to their relevance to the review objective. Randomized controlled trials (RCTs), meta-analyses, and large real-world observational studies were prioritized; relevant reviews and guideline documents were included to contextualize the evidence. Because study designs and endpoints were heterogeneous, the evidence was synthesized using a structured narrative approach (Tables 1–4).

Anti-IgE Therapy (Omalizumab): Impact on Infections and Antiviral Immunity

Omalizumab is the biologic agent with the longest record of clinical use in severe pediatric allergic asthma.^{1,16–18} IgE-mediated signaling through FcεRI can impair antiviral interferon responses in plasmacytoid dendritic cells.^{8,11} By reducing free IgE levels and downregulating FcεRI expression, omalizumab restores interferon-α production and enhances antiviral immunity, as demonstrated in translational studies.²³ Immunological reviews further support the

Table 1 Summary of Main Studies on Omalizumab with Associated Results Included in the Review

First Author, Year	Study Design	Population (Age)	Biologic/ Intervention	Primary Focus	Safety/ Infection-Related Endpoints	Main Findings
Normansell, 2014 ²⁰	Cochrane systematic review	Adults + children	Omalizumab	Efficacy & safety	Severe adverse events	No increase vs placebo (OR: 0.72; CI 95%: 0.57–0.91)
Teach, 2015 ²²	Randomized controlled trial	Children	Omalizumab	Seasonal exacerbation prevention	Virus-triggered exacerbations	Reduced fall exacerbations vs placebo 11.3% vs 21.0%; [OR], 0.48; 95% CI, 0.25–0.92)
Gill, 2018 ²³	Mechanistic clinical study	Children + adults	Omalizumab	Antiviral immunity	Interferon- α production	Omalizumab treatment significantly increased IFN- α responses after IgE cross-linking and stimulation with either rhinovirus (ratio of geometric means, 2.06; 95% CI, 1.20–3.55; P =0.01) or influenza virus (ratio of geometric means, 1.57; 95% CI, 1.09–2.25; P =0.02)

Notes: Omalizumab is a humanized, recombinant IgG1 monoclonal antibody directed against IgE that prevents the binding of free IgE to the high-affinity IgE receptor (Fc ϵ RI) on mast cells and basophils without interacting with receptor-bound IgE. By rapidly reducing circulating free IgE levels, omalizumab downregulates Fc ϵ RI expression on effector cells, thereby attenuating the allergic inflammatory cascade. According to the European Medicines Agency (EMA), omalizumab is approved as add-on therapy for severe allergic asthma in adults, adolescents, and children aged ≥ 6 years.

Abbreviations: OR: odds ratio; CI: confidence interval; IFN: interferon.

role of IgE pathways in antiviral defense.^{42,43} Clinically, Teach et al found that preseasonal omalizumab significantly reduced fall asthma exacerbations in children, particularly during rhinovirus peaks.²² Emerging evidence suggests that omalizumab may reduce exacerbation frequency and attenuate the clinical severity of individual viral episodes, for instance, by restoring interferon-mediated antiviral responses, potentially resulting in shorter or milder illness rather than simply fewer triggering events.^{11,23}

The Cochrane review by Normansell et al found no increase in serious or respiratory infections with omalizumab compared with placebo.²⁰ A recent systematic review of pediatric biologic safety similarly found no increased infectious risk.²¹ Real-world pediatric studies have demonstrated sustained effectiveness and stable safety profiles during long-term omalizumab treatment.^{44,45} During the COVID-19 pandemic, observational data indicated no increased susceptibility to SARS-CoV-2 infection or severe disease among children receiving biologic therapy.^{30–32} Overall, anti-IgE therapy appears to exert immunomodulatory effects without increasing infection risk.

Anti-IL-5 and Anti-IL-5R Therapies (Mepolizumab and Benralizumab): Infectious Safety and Corticosteroid-Sparing Effects

Biologic therapies targeting the IL-5 pathway have been extensively evaluated for infectious safety. The Cochrane review by Farne et al found no evidence of an increased risk of infection-related adverse events or serious adverse events in patients treated with anti-IL-5 therapies.²⁴ In the SIRIUS trial, Bel et al demonstrated a significant oral corticosteroid-sparing effect of mepolizumab in severe eosinophilic asthma.²⁵ Considering the established association between systemic corticosteroid exposure and infection risk,¹² reducing corticosteroid use may indirectly lower infection risk. Pediatric studies have similarly reported favorable safety profiles: Gupta et al demonstrated safe use in children aged 6–11 years,²⁶ and Yancey et al reported consistent findings in adolescents.²⁷ Long-term data indicate sustained benefit without increased infectious complications.²⁸

Phase 3 trials of benralizumab, including SIROCCO and CALIMA, and the long-term BORA extension study demonstrated no increase in infection rates despite profound eosinophil depletion.^{33–35} Additionally, benralizumab did not impair humoral responses to influenza vaccination in adolescents and young adult patients.³⁶ Collectively, these findings indicate that IL-5 pathway inhibition preserves immune competence without increasing susceptibility to infection.

Table 2 Summary of Main Studies on Anti-IL5 Therapies with Associated Results Included in the Review

First Author, Year	Study Design	Population (Age)	Biologic/ Intervention	Primary Focus	Safety/ Infection-Related Endpoints	Main Findings
Farne, 2017/ 2022 ²⁴	Cochrane review	Adults + adolescents	Anti-IL-5 therapies	Safety & efficacy	Clinically significant or serious adverse events	No increased rates vs placebo (mepolizumab clinically significant adverse events: risk ratio 0.45, 95% CI 0.11 to 1.80; participants = 936; studies = 2; $I^2 = 0\%$; Benralizumab clinically significant adverse events: risk ratio 2.15, 95% CI 1.02 to 4.57; serious adverse events: risk ratio 0.81, 95% CI 0.66 to 1.01)
Bel (SIRIUS), 2014 ²⁵	Randomized controlled trial	Adults + adolescents	Mepolizumab	OCS-sparing	OCS-sparing effect	Reduced OCS use in patients on mepolizumab vs placebo (CI 95%, 1.25 to 4.56; $P=0.008$)
Gupta, 2019 ²⁶	Open-label pediatric clinical trial	Children	Mepolizumab	Safety	Adverse events including infections	Favorable safety profile
Yancey, 2019 ²⁷	Pooled analysis of clinical trial data	Adolescents	Mepolizumab	Efficacy & safety	Adverse events including infections	Consistent safety profile
Pavord, 2024 ²⁸	Long-term open-label extension study	Children + adolescents + adults	Mepolizumab	Long-term safety	Adverse events including infections	Favorable benefit:risk for up to ~10 years
Bleecker (SIROCCO), 2016 ³³	Phase 3 RCT	Adults + adolescents	Benralizumab	Efficacy & safety	Infection rates	No increase despite eosinophil depletion
FitzGerald (CALIMA), 2016 ³⁴	Phase 3 RCT	Adults + adolescents	Benralizumab	Efficacy & safety	Infection rates	No increase despite eosinophil depletion
Busse (BORA), 2019 ³⁵	Extension study	Adults + adolescents	Benralizumab	Long-term safety	Serious infections	No new safety signal
Zeitlin (ALIZE), 2018 ³⁶	Phase IIIb trial	Adolescents + young adults	Benralizumab	Vaccine response	Influenza antibody response	Preserved humoral immunity

Notes: Mepolizumab and Benralizumab are monoclonal antibodies targeting the IL-5 pathway. Mepolizumab is a humanized IgG1 κ monoclonal antibody directed against IL-5 that selectively binds circulating IL-5, preventing its interaction with the IL-5 receptor on eosinophils. By inhibiting IL-5 signaling, mepolizumab reduces eosinophil maturation, activation, and survival, thereby decreasing eosinophilic inflammation. According to the European Medicines Agency (EMA), mepolizumab is approved as add-on maintenance therapy for severe refractory eosinophilic asthma in adults, adolescents, and children aged ≥ 6 years. Benralizumab is a humanized IgG1 κ monoclonal antibody directed against the α -subunit of the interleukin-5 receptor (IL-5R α) expressed on eosinophils and basophils. By binding to IL-5R α , benralizumab induces antibody-dependent cell-mediated cytotoxicity (ADCC), resulting in rapid and near-complete depletion of eosinophils. According to the European Medicines Agency (EMA), benralizumab is approved as add-on maintenance therapy for severe eosinophilic asthma in adults and adolescents aged ≥ 12 years.

Abbreviations: RCT: randomized controlled trial; OCS: oral corticosteroids; CI: confidence interval; IL-5: interleukin 5.

Anti-IL-4R α Therapy (Dupilumab): Epithelial Barrier and Infection Outcomes

Dupilumab has demonstrated efficacy and safety in children with moderate-to-severe asthma. In the pivotal randomized trial involving children aged 6–11 years, Bacharier et al reported significant reductions in exacerbations and improved lung function without an increase in respiratory or serious infections.³⁷ Long-term data from the VOYAGE and

Table 3 Summary of Main Studies on Dupilumab with Associated Results Included in the Review

First Author, Year	Study Design	Population (Age)	Biologic/ Intervention	Primary Focus	Safety/Infection-Related Endpoints	Main Findings
Bacharier, 2021 ³⁷	RCT	Children	Dupilumab	Efficacy & safety	Respiratory/serious infections	No clinically relevant safety signal for infections
Bacharier, (VOYAGE), 2024 ³⁸	Extension study	Children	Dupilumab	Lung function	Lung function	Significantly and durably improve lung function
Phipatanakul (EXCURSION), 2024 ³⁹	Open-label extension study	Children	Dupilumab	Long-term efficacy	Safety including infections	No emerging safety concerns

Notes: Dupilumab is a fully human IgG4 monoclonal antibody directed against the interleukin-4 receptor alpha (IL-4Rα) subunit, thereby inhibiting signaling of both IL-4 and IL-13, two key cytokines involved in type 2 inflammation. By blocking the IL-4/IL-13 pathway, dupilumab reduces type 2 inflammatory responses, including eosinophilic airway inflammation and IgE production. According to the European Medicines Agency (EMA), dupilumab is approved as add-on maintenance therapy for severe asthma with type 2 inflammation, characterized by raised blood eosinophils and/or elevated fractional exhaled nitric oxide (FeNO), in adults, adolescents, and children aged ≥6 years who are inadequately controlled despite high-dose inhaled corticosteroids plus another maintenance treatment.

Abbreviation: RCT: randomized controlled trials.

Table 4 Summary of Main Studies on Tezepelumab with Associated Results Included in the Review

First Author, Year	Study Design	Population (Age)	Biologic/ Intervention	Primary Focus	Safety/Infection-Related Endpoints	Main Findings
Menzies-Gow (NAVIGATOR), 2021 ²⁹	Phase 3 RCT	Adults + adolescents	Tezepelumab	Exacerbation reduction	Serious infections	No increase of serious infections vs placebo
Corren, 2022 ⁴⁰	Post hoc analysis	Adults + young adults	Tezepelumab	Biomarker response	Biomarker response	Efficacy across phenotypes
Lugogo (PASSAGE), 2025 ⁴¹	Real-world observational study	Adults + adolescents	Tezepelumab	Effectiveness & safety	Infection rates	Stable real-world safety

Notes: Tezepelumab is a fully human IgG2λ monoclonal antibody directed against thymic stromal lymphopoietin (TSLP), an epithelial-derived cytokine that acts as an upstream regulator of multiple inflammatory pathways involved in asthma pathogenesis. By binding to TSLP, tezepelumab prevents its interaction with the TSLP receptor complex, thereby reducing activation of downstream immune responses, including type 2 and non-type 2 inflammatory pathways. According to the European Medicines Agency (EMA), tezepelumab is approved as add-on maintenance therapy for severe asthma in adults and adolescents aged ≥12 years who are inadequately controlled despite high-dose inhaled corticosteroids plus another maintenance treatment.

Abbreviation: RCT, randomized controlled trials.

EXCURSION programs confirmed sustained efficacy and stable safety profiles.^{38,39} Mechanistically, IL-4 and IL-13 contribute to epithelial barrier dysfunction in asthma.⁷ Direct evidence that dupilumab reduces infection incidence remains limited; however, improved epithelial barrier integrity and reduced corticosteroid exposure may help preserve respiratory immune homeostasis. However, this proposed mechanism remains largely hypothetical and is supported by limited data in pediatric asthma.

Upstream Biologics (Tezepelumab): Immunomodulation and Safety

Tezepelumab targets thymic stromal lymphopoietin (TSLP) and acts upstream of multiple inflammatory pathways. In the NAVIGATOR trial, Menzies-Gow et al reported significant reductions in exacerbation rates without an increase in respiratory or serious infections.²⁹ Post hoc analyses confirmed consistent safety across inflammatory phenotypes.⁴⁰ Emerging real-world evidence from the PASSAGE study showed sustained clinical effectiveness and stable infection rates.⁴¹ Although current evidence supports the infectious safety of upstream TSLP blockade, long-term pediatric data are less extensive than those for other biologic agents, warranting cautious interpretation and further dedicated studies in children and adolescents.

Biologic Therapies and SARS-CoV-2 Infection

The COVID-19 pandemic provided real-world evidence on infectious safety in pediatric asthma. Multinational cohort data indicated that children with asthma did not experience disproportionately severe COVID-19 outcomes.³⁰ Observational studies of children receiving biologics found no increased susceptibility to SARS-CoV-2 infection or severe disease.³¹ These findings support continuing biologic therapy during viral infections when clinically appropriate.¹

Discussion and Conclusions

This structured narrative review highlights that biologic therapies for severe pediatric asthma provide effective disease control while maintaining a favorable infectious safety profile.^{16–18,20,21} A central finding is the distinction between immunomodulation and immunosuppression. In contrast to systemic corticosteroids, which are associated with systemic adverse effects, including growth impairment,^{12,13} biologics selectively target key inflammatory pathways while preserving overall immune competence and host defense. Among the available biologics, anti-IgE therapy has the strongest evidence of direct effects on antiviral immunity. Experimental and translational studies link IgE signaling to impaired antiviral responses and indicate that omalizumab can restore interferon-mediated pathways.^{11,23,42} Clinically, omalizumab reduces virus-triggered exacerbations without increasing infection risk.^{20–22,44,45}

Other biologic classes appear to affect infection risk primarily through indirect mechanisms. Anti-IL-5/IL-5R therapies do not increase infection rates,^{24,26–28,33–35} and their corticosteroid-sparing effects may reduce treatment-related toxicity and the infection risk associated with prolonged corticosteroid exposure.^{12,13,25} These therapies deplete eosinophils, which contribute to host defense against helminthic parasites. The prescribing information for the other biologics discussed in this review includes related, although mechanistically distinct, warnings. Omalizumab labeling recommends monitoring patients at high risk of helminth infection because IgE contributes to anti-helminth immunity.⁴⁶ Dupilumab and tezepelumab labeling recommends treating pre-existing helminth infections before therapy and discontinuing treatment if an infection develops and fails to respond to anti-helminth therapy, reflecting the roles of Th2 cytokine signaling and TSLP to host defense against helminths.^{47,48} Herpes zoster has been reported in a small number of patients receiving mepolizumab or benralizumab in clinical trials, and case reports suggest a possible class effect among anti-IL-5/IL-5R agents.^{33,49,50} In contrast, pooled trial data for dupilumab have shown lower rates of herpes zoster and eczema herpeticum than placebo.^{51–53} Similarly, dupilumab demonstrates sustained efficacy and safety without increased infectious burden.^{37–39} Tezepelumab further reinforces this paradigm, with consistent reductions in exacerbations and no evidence of increased infections across clinical trials and early real-world data.^{29,40,41}

Because infection-related outcomes are rarely evaluated as primary endpoints, the available evidence remains largely indirect and should be interpreted cautiously. Reductions in infection burden reported in some studies may reflect better asthma control, fewer exacerbations, and reduced systemic corticosteroid exposure rather than a direct anti-infective effect of biologic therapy. These factors may nevertheless improve overall respiratory health.

Evidence from the COVID-19 pandemic provides additional reassurance: children receiving biologic therapy did not have greater susceptibility to SARS-CoV-2 infection or worse clinical outcomes,^{30–32} supporting current guideline recommendations to continue treatment during viral infections.^{1,16} Overall, biologic therapies represent an effective and immunologically balanced approach to severe pediatric asthma by combining targeted disease control with preserved host defense. However, the evidence is limited by the absence of infection-specific endpoints, heterogeneity in study designs and outcome definitions, and insufficient long-term pediatric data. Furthermore, no head-to-head trials have directly compared infection-related outcomes across biologic classes, and safety data are particularly limited for newer agents, such as tezepelumab. In addition, most evidence derives from post hoc analyses and observational studies, with infection-related outcomes typically reported as secondary findings; potential ascertainment and reporting bias should therefore be considered.

This narrative synthesis is not intended to guide management decisions in individual clinical scenarios, for which case-specific clinical judgment and specialist input remain essential. As with any narrative review, the approach is inherently more susceptible to selection and interpretation bias than a systematic review or meta-analysis; the findings should therefore be considered hypothesis-generating rather than a basis for individual treatment decisions. Prospective

studies incorporating standardized infection-related outcomes, biomarkers of antiviral immunity, and extended follow-up are needed to define long-term immune effects more clearly and support biologic selection within precision-medicine strategies.

Disclosure

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