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A COMPREHENSIVE REVIEW OF ADVERSE EFFECTS OF BIOLOGICAL TREATMENT IN ASTHMA

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ABSTRACT

Background: Biologic therapies have revolutionized the treatment of severe asthma by targeting specific inflammatory pathways, reducing exacerbation rates, improving lung function, and decreasing dependence on systemic corticosteroids. Despite their proven efficacy, concerns regarding adverse effects may limit their acceptance and early implementation in clinical practice.

Objective: This review aimed to evaluate and summarize the adverse effects associated with currently approved biologic agents for asthma treatment, including omalizumab, benralizumab, mepolizumab, dupilumab, and tezepelumab.

Methods: A narrative literature review was conducted using the PubMed database. English-language studies published between January 2011 and May 2026 were analyzed, including randomized controlled trials, systematic reviews, meta-analyses, observational studies, and selected case reports. Particular attention was paid to the incidence and clinical significance of hypersensitivity reactions, infections, eosinophilia, cardiovascular events, and malignancies.

Results: The reviewed biologics demonstrated favorable safety profiles, with most adverse events being mild to moderate and rarely leading to treatment discontinuation. Omalizumab was associated with a rare risk of anaphylaxis, while dupilumab was linked to transient eosinophilia and uncommon eosinophilic complications. Benralizumab, mepolizumab, and tezepelumab showed reassuring long-term safety data, with no significant increase in severe infections, malignancies, or cardiovascular events. Across all agents, the incidence of serious adverse reactions remained low.

Conclusions: Current evidence indicates that the clinical benefits of biologic therapies in severe asthma substantially outweigh their potential risks. Improved awareness of their safety profiles may reduce patient concerns and facilitate earlier treatment initiation, reduce corticosteroid-related complications, and contribute to better long-term outcomes and quality of life in patients with severe asthma.

KEYWORDS

Severe asthma, Biologic therapy, Adverse effects, Safety profile

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Introduction

Asthma is a chronic inflammatory disease of the airway affecting more than 300 million individuals worldwide and constituting a major global public health challenge. Despite significant advances in pharmacological management, a considerable proportion of patients continue to experience poor symptom control, recurrent exacerbations, progressive decline in lung function, and impaired quality of life.

The growing understanding of asthma pathophysiology has revealed the heterogeneous nature of the disease and enabled the identification of distinct inflammatory endotypes. In particular, type 2 (T2)-high inflammation, characterized by increased activity of immunoglobulin E (IgE), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-13 (IL-13), and thymic stromal lymphopoietin (TSLP), has become a primary therapeutic target. These discoveries have led to the development of biologic therapies designed to selectively interfere with key inflammatory pathways responsible for persistent airway inflammation and exacerbation risk.

Biological agents revolutionized the treatment of severe asthma. Clinical trials have demonstrated significant reductions in asthma exacerbation rates, improvement of lung function and decreased oral corticosteroid dependence in adults and children with moderate-to-severe asthma. All these factors improve the quality of life of patients with asthma. Despite indisputable advantages of biological treatment, some adverse effects of these drugs have been described.

Side effects and their frequency vary depending on the type of drug and its mechanism of action. The aim of the study is to collect side effects of five biological agents - omalizumab, benralizumab, mepolizumab, dupilumab and tezepelumab. Two of them (benralizumab and mepolizumab) act by inducing depletion of eosinophils in blood and tissues in eosinophilic asthma. Omalizumab acts by neutralizing free immunoglobulins IgE crucial in allergic asthma. Dupilumab works by blocking interleukin: IL-4 and IL-13,

effectively stopping the inflammatory cascade that causes asthma symptoms. Tezepelumab inhibits thymic stromal lymphopoietin (TSLP) in the inflammatory cascade.

Early admission of this therapy is really important, because it improves prognosis and reduces harmful impact of systemic corticosteroids like osteoporosis, diabetes mellitus, hypertension, ulcer disease, obesity, cataract and increased susceptibility to infections. That's why patients should be fully informed about the safety of biological treatment based on clinical research and reliable literature review. The aim of this narrative review is to increase knowledge and provide reliable information to help to make clinical decisions. We believe that reducing patients' fear of new and unfamiliar therapy will enable it to be started earlier.

Methodology

A narrative literature review was conducted to evaluate the adverse effects associated with biological therapies used in the treatment of bronchial asthma, with particular emphasis on severe eosinophilic and allergic asthma phenotypes. The review aimed to summarize the current evidence regarding the safety profile, frequency, and clinical relevance of adverse drug reactions related to monoclonal antibody therapies.

The literature search was performed using the electronic database PubMed. Articles published between January 2011 and May 2026 were included in order to capture contemporary evidence concerning currently approved biologic agents for asthma management.

The search strategy included combinations of the following Medical Subject Headings (MeSH) terms and keywords: 'bronchial asthma', 'severe asthma', 'biological therapy', 'biologic agents', 'monoclonal antibodies', 'adverse effects', 'drug-related side effects', 'safety profile', 'omalizumab', 'mepolizumab', 'benralizumab', 'dupilumab', and 'tezepelumab'.

Eligible studies included randomized controlled trials, systematic reviews, meta-analyses, observational studies, case reports and case studies published in English. Case reports and conference abstracts without full-text availability were excluded.

Particular attention was paid to the incidence and type of adverse events, including hypersensitivity reactions, injection-site reactions, eosinophilia, infections, cardiovascular complications, malignancies and other clinically significant safety concerns.

Results

1. Omalizumab

Anaphylaxis

As the most dangerous side effect of Omalizumab an anaphylaxis is listed. However the studies show low risk of anaphylaxis - at approximately 0.09% of patients receiving omalizumab [1]

In a retrospective case-control study designed to further characterize and identify risk factors for anaphylaxis to omalizumab, 51% of 123 reported cases occurred after the first dose; 72% occurred during the first three doses. Furthermore, a history of anaphylaxis unrelated to omalizumab use was found to be a risk factor for development of anaphylaxis in response to omalizumab (odds ratio = 8.1 [95% CI = 2.7-24.3]). Most patients who develop anaphylaxis to omalizumab are female (84%), though this association has not been described with other biologic agents. [2]

The Food and Drug Administration (FDA) decided that self-administration of omalizumab outside the health care setting should be considered in select patients. Patient-specific factors for self-administration would include: initiation and receipt of at least 3 doses in a health care setting, no history of anaphylaxis in response to omalizumab or other agents, and assurance that the patient or caregiver is able to treat anaphylaxis appropriately with a readily available epinephrine auto-injector.

Serum sickness-like reactions (SSLRs):

In omalizumab pre-marketing clinical trials, there were four reported incidents of SSLRs. Three cases developed in patients receiving omalizumab and one in the control group [3] Signs and symptoms included arthritis, rash, fever, and lymphadenopathy with an onset 1–5 days after the first or subsequent injections of omalizumab. All cases resolved despite the continuation of treatment. The first case of serum sickness reaction

leading to drug discontinuation was described in 2007 in a 67-year-old woman receiving omalizumab 300 mg for severe persistent asthma. Symptoms of arthralgia and swelling of the left wrist and lower extremities, malaise and generalized pruritus developed on day 5 post injection. She was found to have left wrist and ankle arthritis, pitting edema of the lower extremities and tenosynovitis of the left-hand extensors. Symptoms self-resolved; however, they recurred 6 days after an additional dose of omalizumab 300 mg. [4]

Infections

Another potential side effect is increased risk of geohelminth infections. There are insufficient data to clearly draw any conclusions regarding the risk of geohelminth infections in those receiving omalizumab. One randomized, double-blind, placebo-controlled trial conducted in Brazil enrolled 137 patients who received either omalizumab or placebo for 52 weeks. The cohort receiving omalizumab did not have a significantly higher risk of helminth infection (odds ratio = 1.47; 95% CI = 0.74-2.95). In addition, infection severity and response to anthelmintic therapies did not appear to be influenced by omalizumab therapy. [5]

Eosinophilia

Multiple case reports describe the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) after treatment with omalizumab for severe asthma, and this risk is included on omalizumab product label. It was considered if EGPA is not caused by reducing systemic corticosteroid during omalizumab treatment, and it has been suggested that this may reflect an “unmasking” of EGPA. However there are reports of patients who developed Churg–Strauss syndrome after and were not treated with long-term oral corticosteroids [6]

Routine monitoring of eosinophil counts is not required, but there should be a low threshold to investigate eosinophil counts if a patient develops worsening respiratory symptoms, rash, myalgias, neuropathy, or other potential manifestations of hypereosinophilia while on omalizumab.

Malignancy

There is a theoretical concern as to whether omalizumab may be associated with increased risk of malignancy. Prospective, observational cohort study (Epidemiologic Study of Xolair - Omalizumab: Evaluating Clinical Effectiveness and Long-term Safety in Patients with Moderate-to-Severe Asthma [EXCELS]), which included 7857 patients, compared the incidence of malignancies over a 5-year period for patients taking omalizumab at baseline with those having no history of omalizumab treatment. The hazard ratio (omalizumab vs nonomalizumab) after adjustment for confounders and risk factors was 1.09 (95% CI = 0.87-1.38) for all malignancies. Thus, EXCELS data analysis suggested that omalizumab therapy is not related to an increase in risk of malignancies. [7]

Cardiovascular events

Following concerns regarding malignancies, a numeric imbalance in various cardiovascular and cerebrovascular events was also observed in those receiving omalizumab. The cardiovascular and/or cerebrovascular serious adverse events (SAEs) included myocardial infarction, unstable angina, transient ischemic attack, pulmonary embolism and/or venous thrombosis, pulmonary hypertension, ischemic stroke, and cardiovascular-related death. [8]

To evaluate potential SAEs related to omalizumab use, a pooled analysis was conducted, which included data from 25 randomized controlled trials involving 3342 omalizumab-treated patients and 2895 placebo-treated patients. The overall incidence rates of arterial thrombotic events (myocardial infarction, stroke, transient ischemic attack, and unstable angina) per 1000 patient years of observation time for omalizumab- and placebo-treated patients were 2.7 (95% CI = 0.88-6.3) and 2.4 (95% CI = 0.65-6.1), respectively. The rate difference was 0.30 (95% CI = -4.2-4.6), thus indicating that the incidence rates for arterial thromboembolic events were similar in both groups. However, the analysis had limitations, including unmeasured confounders, low numbers of events, and wide confidence intervals, all of which limit the capability to exclude small differences in risk. [9]

2. Mepolizumab

Mepolizumab has demonstrated a consistent safety profile in randomized placebo-controlled trials. Five studies were analyzed: DREAM (Dose Ranging Efficacy And Safety With Mepolizumab in Severe Asthma) [10], MENSA (Efficacy and Safety Study of Mepolizumab Adjunctive Therapy in Subjects With Severe Uncontrolled Refractory Asthma) [11], SIRIUS (Mepolizumab Steroid-Sparing Study in Subjects With Severe Refractory Asthma) [12] and MUSCA (Efficacy and Safety Study of Mepolizumab Adjunctive Therapy in Participants With Severe Eosinophilic Asthma on Markers of Asthma Control) [13]. Additionally, in COSMOS (A Study to Determine Long-term Safety of Mepolizumab in Asthmatic Subjects), a 52-week open-label extension study of MENSA and SIRIUS, mepolizumab had a favorable safety profile, with no increase in the rate of adverse events over the study period or compared with previous placebo-controlled trials. [14]

Although mepolizumab has demonstrated a favorable safety profile in placebo-controlled trials of up to 12 months' duration and in an open-label extension study, long-term safety data in patients with severe eosinophilic asthma beyond 1.5 years are lacking. The COLUMBA study is the continuation of the DREAM study. This is the first study to report data evaluating the long-term durability and safety of the anti-IL-5 biologic mepolizumab in patients with severe eosinophilic asthma. It was conducted between September 28, 2012, and May 31, 2017, in 65 centers across 13 countries.

According to the COLUMBA (Open-label Long Term Extension Safety Study of Mepolizumab in Asthmatic Subjects) study the most frequently reported on-treatment adverse events were respiratory tract infection, headache, bronchitis, and asthma worsening. As expected, respiratory tract infections were reported more frequently in patients who had chronic rhinosinusitis at screening. Overall, 347 patients were enrolled for an average of 3.5 years. Eight patients (2%) experienced allergic/hypersensitivity systemic reactions, and 1 patient (<1%) experienced a non-allergic systemic reaction. There were no reports of mepolizumab-related anaphylaxis. Twenty-four (7%) patients experienced an on-treatment opportunistic infection, of whom 8 (2%) patients experienced herpes zoster infection, 1 event was reported as serious. No parasitic infections were reported. Six (2%) patients reported malignancies while receiving treatment: 3 (<1%) patients had basal cell carcinoma, 2 (<1%) patients had prostate cancer and 1 (<1%) patient had breast cancer. The number of cancers observed in the study population was similar to age- and sex-adjusted incidence rates from the Surveillance Epidemiology and End Results Registry. There were no reports of clinically significant changes in electrocardiographic findings or laboratory data, and vital signs remained stable throughout the study. Overall, no new safety concerns were identified in this study after long-term exposure. [15]

3. Benralizumab

The most common side effects of benralizumab are viral upper respiratory tract infection, worsening asthma, pneumonia, hypersensitivity reactions (urticaria rash). Anaphylaxis was not described. The randomized, double-blind, parallel-group study was conducted to assess the long-term safety and efficacy of benralizumab for patients with severe, uncontrolled eosinophilic asthma. 1576 patients treated with benralizumab were included in the BORA phase 3 extension trial. The most common adverse events in all groups were viral upper respiratory tract infection (14–16%) and worsening asthma (7–10%). The most common serious adverse events were worsening asthma (3–4%), pneumonia (<1% to 1%), and pneumonia caused by bacterial infection (0–1%). The 2 years of safety results validate that observations observed in the first year of benralizumab continued through a second year of treatment. No new consequences of long-term eosinophil depletion occurred, and the incidence of other adverse events, including opportunistic infections, were similar during the second year. [16]

There is no evidence that persistently low or absent eosinophil counts, as a result of pharmacological targeting, result in an increased incidence of cancer. Results observed in patients with severe asthma treated with benralizumab during the approximately 1-year placebo-controlled and 56-week extended treatment periods (4/1663 [0.24%] and 12/1576 [0.8%], respectively). The incidence of malignancy for patients continuously exposed to benralizumab from the start of the controlled treatment period through the end of the extension period (up to 2 years) was 8/1030 (0.8%). [17]

Cardiovascular risk

The nationwide observational study in Belgium shows that biologic therapies for patients with severe asthma were associated with a significantly lower risk of all-cause mortality and specific cardiovascular diseases compared with non-biologic users. This cohort study consisted of 171,865 patients (mean age 64 years; 55% females) including 1826 (1.1%) anti-IgE users and 2398 (1.4%) anti-IL5/IL5R users. Anti-IgE exposure (omalizumab) was associated with a significantly lower risk of mortality (HR 0.48, 95% CI 0.40-0.58), congestive heart failure (HR 0.79, 95% CI 0.65-0.95), peripheral artery disease (HR 0.66, 95% CI 0.51-0.86), and stroke (HR 0.54, 95% CI 0.36-0.81). Anti-IL5/IL5R use (mepolizumab or benralizumab) was associated with a significantly lower risk of mortality (HR 0.35, 95% CI 0.29-0.42), congestive heart failure (HR 0.63, 95% CI 0.52-0.76), arrhythmia (HR 0.78, 95% CI 0.68-0.90), and peripheral artery disease (HR 0.69, 95% CI 0.54-0.87) compared with non-biologic users. No significant differences in the risk of myocardial infarction and pulmonary embolism were observed. [18]

4. Dupilumab

Dupilumab safety profile in asthma trials has been favorable and is generally similar to that of placebo, aside from injection-site reactions. In pooled analyses of asthma studies, the common adverse events of dupilumab with incidence $\geq 1\%$ were injection-site erythema, nasopharyngitis, and oropharyngeal pain. Injection-site reactions are usually mild in nature and characterized by transient redness or itching. Unlike in atopic dermatitis, where up to 10% of patients experience conjunctivitis or other ocular effects with dupilumab, the incidence of conjunctivitis in asthma patients is not a significant concern. Similarly, rates of headache, sinusitis, and upper respiratory tract infections were found to be comparable between dupilumab and placebo in controlled trials, and these are mostly related to the underlying disease or co-administered inhalation therapies. [19]

Severe hypersensitivity reactions to dupilumab are uncommon. Anaphylaxis due to dupilumab was not observed in asthma trials [20]

A few cases of generalized urticaria or serum sickness-like reactions have been described, so dupilumab is contraindicated in patients with known dupilumab allergy. Any signs of severe hypersensitivity require immediate discontinuation of treatment and prompt medical evaluation to assess allergenicity. However, these events are very rare considering the large population of patients treated. [21]

With respect to vaccinations, since dupilumab modulates immune function, live vaccines are generally not recommended during treatment due to the theoretical risk of inadequate immune response. Non-live vaccines, such as influenza or COVID-19 vaccines, are considered safe, and patients should stay up-to-date with them. Consolidating on this, only a few studies have shown that dupilumab does not significantly impair the antibody response to vaccines [22]

Hypereosinophilia has been observed in 4%-25% of patients treated with dupilumab and is transient in most cases, although there have been reports of persistent cases of symptomatic hypereosinophilia consistent with eosinophilic granulomatosis with polyangiitis (EGPA), eosinophilic pneumonia, eosinophilic vasculitis, and sudden worsening of asthma symptoms. The mechanism of dupilumab-induced hypereosinophilia is the blockade of the IL-4/IL-13 pathway which reduce eosinophil migration and accumulation in blood by inhibiting eotaxin-3, VCAM-1 (Vascular Cell Adhesion Molecule) and TARC (Thymus and Activation-Regulated Chemokine) without simultaneously inhibiting eosinophilopoiesis in bone marrow. [23]

Recent studies suggest that patients with atopic dermatitis receiving dupilumab are at a higher risk of developing cutaneous lymphoma. The population-based cohort study on patients in the United States aimed to investigate the risk of lymphoma among patients with asthma receiving dupilumab. A total of 14 936 dupilumab-treated and 734 126 inhalation corticosteroids plus long-acting β -agonists-treated patients with asthma were included. After propensity score matching, dupilumab-treated patients were found to have a higher risk of lymphoma (54 *versus* 43 cases, hazard ratio (HR) 1.79, 95% CI 1.19-2.71), especially T-cell and natural killer (NK)-cell lymphomas (19 *versus* ≤ 10 cases, HR 4.58, 95% CI 1.82-11.53). There was no significant difference in incidence of other malignant neoplasms. Dupilumab was also associated with significantly lower all-cause mortality (328 *versus* 793 deaths, HR 0.65, 95% CI 0.57-0.74). [24]

5. Tezepelumab

The most common adverse effects of tezepelumab are infections. There were no cases of anaphylaxis reported. Clinical trials also show that tezepelumab does not increase the risk of malignancies.

In the study PASSAGE overall 208 participants were included in the interim analysis. In total, 16 participants (7.7%) reported a serious adverse event (SAE) during the treatment period after tezepelumab initiation. Treatment discontinuation due to an SAE was reported in one participant. No deaths were reported. Infections and infestations were the most common class of SAEs, reported by eight participants (3.8%), followed by respiratory, thoracic and mediastinal disorders, reported by four participants (1.9%) [25]

In the NAVIGATOR study 1061 patients underwent randomization (529 were assigned to receive tezepelumab and 532 to receive placebo). The frequencies and types of adverse events did not differ meaningfully between the two groups. A total of 77.1% of the patients in the tezepelumab group and 80.8% of those in the placebo group reported an adverse event, and 9.8% and 13.7% reported a serious adverse event, respectively. The percentage of patients who discontinued owing to adverse events was 2.1% in the tezepelumab group and 3.6% in the placebo group. The most common adverse events were nasopharyngitis, upper respiratory tract infection, headache, and asthma (which was more frequently observed in the placebo group than in the tezepelumab group). The incidence of severe infections did not differ between the trial groups (46 patients [8.7%] in each group), nor did the incidence of cancer (4 patients [0.8%] in each group). Two deaths were reported during the trial period (one from heart failure and one of unknown cause); both were in the placebo group. Injection-site reactions occurred in 3.6% of the patients in the tezepelumab group and in 2.6% of those in the placebo group. No treatment-related anaphylactic reactions or cases of Guillain-Barré syndrome were reported. [26]

Tables 1 and 2 summarize the above results.

Table 1. Major adverse events and safety outcomes reported for biologic therapies used in severe asthma

Biologic agent	Key studies	Sample size	Most frequent adverse events	Serious adverse events	Malignancy findings	Key safety conclusion
Omalizumab	EXCELS, pooled RCT analyses	7,857 patients (EXCELS) 3,342 treated patients in pooled RCTs	Injection-site reactions, mild hypersensitivity reactions	Anaphylaxis (~0.09%); serum sickness-like reactions; rare EGPA cases	HR for malignancy 1.09 (95% CI 0.87–1.38)	Extensive long-term evidence supports a favorable safety profile
Mepolizumab	DREAM, MENSA, SIRIUS, MUSCA, COSMOS, COLUMBA	347 patients in COLUMBA extension study	Respiratory tract infections, headache, bronchitis, asthma worsening	Hypersensitivity reactions (2%); opportunistic infections (7%); herpes zoster (2%), no anaphylaxis	Malignancies reported in 2% of patients, consistent with expected population rates	No new safety concerns identified after a mean follow-up of 3.5 years
Benralizumab	BORA extension study	1,576 patients	Viral upper respiratory tract infections (14–16%), asthma worsening (7–10%)	Pneumonia (<1–1%); hypersensitivity reactions; no anaphylaxis	Malignancy incidence 0.8% after up to 2 years of treatment	Sustained eosinophil depletion was not associated with additional safety risks
Dupilumab	The Liberty Asthma Quest, Pooled asthma trials; U.S. population-based cohort study	1902 dupilumab-treated patients	Injection-site erythema, nasopharyngitis, oropharyngeal pain	Hypereosinophilia (4–25%); rare EGPA, eosinophilic pneumonia, vasculitis	Increased lymphoma risk reported (HR 1.79; 95% CI 1.19–2.71)	Generally favorable safety profile; eosinophilia requires monitoring
Tezepelumab	PASSAGE; NAVIGATOR	208 patients (PASSAGE); 1,061 patients (NAVIGATOR)	Nasopharyngitis, upper respiratory tract infection, headache	SAEs: 7.7% (PASSAGE); no treatment-related anaphylaxis	Cancer incidence 0.8%, comparable to placebo	Safety profile comparable to placebo, with low discontinuation rates

Table 2. Comparison of selected serious safety outcomes among biologic therapies for severe asthma

Safety outcome	Omalizumab	Mepolizumab	Benralizumab	Dupilumab	Tezepelumab
Anaphylaxis	Rare (~0.09%)	Not reported	Not reported	Not reported	Not reported
Hypersensitivity reactions	Yes	Rare (2%)	Rare	Rare	Rare
Eosinophilia EGPA	Rare reports	Not significant	Not significant	Hypereosinophilia (4–25%); rare EGPA	Not reported
Opportunistic infections	Not confirmed	7%	Not increased	Not increased	Not increased
Malignancy signal	Not confirmed	Not confirmed	Not confirmed	Possible lymphoma signal	Not confirmed
Cardiovascular risk increase	Not demonstrated	Not demonstrated	Not demonstrated	Not demonstrated	Not demonstrated
Long-term safety data available	Extensive (>15 years)	Up to 3.5 years	Up to 2 years	Moderate	Limited
Overall benefit-risk balance	Favorable	Highly favorable	Highly favorable	Favorable	Highly favorable

Abbreviations: EGPA – eosinophilic granulomatosis with polyangiitis; HR – hazard ratio; CI – confidence interval; RCT – randomized controlled trial; SAE – serious adverse event.

Discussion

Biological therapies have substantially transformed the management of severe asthma by targeting specific inflammatory pathways and providing effective alternatives to long-term systemic corticosteroid treatment. The present narrative review summarizes the current evidence regarding the safety profiles of five biologic agents approved for asthma treatment: omalizumab, benralizumab, mepolizumab, dupilumab, and tezepelumab. Overall, the available literature indicates that these therapies are generally well tolerated, with most adverse events being mild to moderate in severity and rarely leading to treatment discontinuation.

Among the reviewed agents, omalizumab has the longest post-marketing experience and the most extensively characterized safety profile. Although anaphylaxis remains the most serious adverse event associated with omalizumab, its incidence is very low, estimated at approximately 0.09%. Importantly, the majority of cases occur within the first three administrations, supporting current recommendations for careful monitoring during treatment initiation. Concerns regarding malignancy and cardiovascular events have been investigated in large observational studies and pooled analyses, which have not demonstrated a statistically significant increase in risk. Nevertheless, the available evidence does not entirely exclude small differences in risk, and continued pharmacovigilance remains warranted.

Benralizumab and mepolizumab, both targeting the eosinophilic inflammatory pathway, demonstrated favorable long-term safety profiles. Despite profound and sustained eosinophil depletion, no evidence has emerged suggesting increased susceptibility to opportunistic infections, malignancies, or other complications associated with immunosuppression. Respiratory tract infections, headache, bronchitis, and asthma exacerbations were the most frequently reported adverse events, consistent with the underlying disease burden in patients with severe asthma. Notably, no cases of treatment-related anaphylaxis were reported in long-term extension studies.

Dupilumab presents a distinct safety profile due to its mechanism of action targeting IL-4 and IL-13 signaling. Injection-site reactions remain the most common adverse event, while severe hypersensitivity

reactions are uncommon. A clinically relevant observation is the occurrence of transient blood eosinophilia, reported in a substantial proportion of treated patients. Although most cases are asymptomatic, rare reports of eosinophilic granulomatosis with polyangiitis, eosinophilic pneumonia, and eosinophilic vasculitis highlight the need for clinical vigilance, particularly in patients who develop worsening respiratory symptoms or systemic manifestations. Furthermore, emerging epidemiological evidence suggesting a possible association between dupilumab use and lymphoma requires further investigation. Although causality has not been established, clinicians should remain aware of this signal until additional long-term data become available.

Tezepelumab, the newest biologic agent included in this review, demonstrated a reassuring safety profile in both clinical trials and real-world studies. The incidence of serious adverse events, infections, malignancies, and treatment discontinuations was comparable to placebo, with no reports of treatment-related anaphylaxis. These findings are particularly encouraging given the broad upstream mechanism of TSLP inhibition and support the use of tezepelumab across diverse asthma phenotypes.

The findings of this review have important clinical implications. Fear of adverse effects may delay initiation of biologic therapy in eligible patients, resulting in prolonged exposure to systemic corticosteroids and their well-established complications, including osteoporosis, diabetes mellitus, hypertension, obesity and cardiovascular disease. Patient education regarding the favorable safety profiles of these agents may improve treatment acceptance and facilitate earlier implementation of biologic therapy.

Conclusions

Biologic therapies have significantly improved the management of severe asthma while maintaining favorable safety profiles. The majority of adverse events are mild and manageable, whereas serious complications occur infrequently. Current evidence indicates that the benefits of biologic treatment substantially outweigh the potential risks, particularly when compared with long-term systemic corticosteroid use. Among the reviewed agents, omalizumab, benralizumab, mepolizumab, dupilumab, and tezepelumab all demonstrated acceptable safety profiles, although specific adverse effects differ according to their mechanisms of action. Long-term studies of mepolizumab and benralizumab confirm sustained safety without evidence of clinically significant consequences associated with prolonged eosinophil depletion. Omalizumab and dupilumab-associated eosinophilia requires clinical awareness and monitoring, although severe eosinophilic complications remain uncommon. Continued long-term monitoring is necessary to identify rare adverse events and further optimize patient selection.

Further research should focus on head-to-head comparisons of biologic therapies, identification of patient-specific risk factors for adverse events, and continued long-term surveillance to detect rare safety signals that may emerge with prolonged use.

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