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Efficacy and Safety of Allergen-Specific Immunotherapy and Biologic Agents in Respiratory Allergies: A Literature Review

Anna Karolina Andrade Moura

mouraannakarolina@gmail.com

Centro Universitário Unifaminas

Luciana de Andrade Agostinho

Centro Universitário Unifaminas

Igor Vilaça Lima Romano

Centro Universitário Unifaminas

Mariana de Almeida Azevedo

Centro Universitário Unifaminas

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Abstract

Methods

A literature review was conducted using articles published between 2014 and 2024 and indexed in the PubMed and SciELO databases to examine the efficacy and safety of allergen-specific immunotherapy and biologic medications. The findings were synthesized descriptively; no formal risk-of-bias assessment or meta-analysis was performed.

Results

The studies reviewed indicated that biologic agents, such as dupilumab, mepolizumab, and omalizumab, may be effective in severe cases, with symptom reduction and generally favorable safety profiles. Subcutaneous and sublingual immunotherapy also showed clinical benefits and a generally satisfactory safety profile, including reports of sustained effects over time.

Discussion

The comparison between the two therapeutic strategies indicates that treatment selection should consider patient characteristics, disease severity, and treatment objectives. Biologic agents may be appropriate in severe cases, whereas immunotherapy may support sustained disease control and immunomodulation.

Conclusion

Both approaches may have a role in the management of respiratory allergies. Individualized treatment and further research on biomarkers and combination strategies may help improve outcomes.

Introduction

Immunology, an essential branch of the biological sciences, focuses on the study of the body's defense mechanisms and is fundamental to understanding allergic reactions and developing increasingly specific therapeutic strategies. The immune system comprises two main components: innate immunity, which provides immediate protection against harmful agents, and adaptive immunity, which mounts more specific and long-lasting responses and is responsible for antibody production, including immunoglobulins (Igs). Among these, immunoglobulin E (IgE) plays a central role in allergic responses mediated by type I hypersensitivity [1, 2].

The regulation of this immune response requires regulatory mechanisms that prevent excessive or autoimmune reactions. These mechanisms include regulatory T cells (Tregs), immunosuppressive

cytokines such as IL-10 and TGF-β, and immune checkpoint molecules, such as CTLA-4 and PD-1, which modulate T-cell activation [3].

When this balance is disrupted, allergic manifestations may arise as a result of type I hypersensitivity reactions. This immediate immune response occurs when IgE, previously produced in response to an allergen, binds to high-affinity receptors on mast cells and basophils. Activation of these cells leads to the release of histamine and other inflammatory mediators, resulting in symptoms such as rhinitis, asthma, urticaria, and conjunctivitis and, in more severe cases, anaphylaxis [4, 3].

Type I hypersensitivity comprises two phases. The first, known as the sensitization phase, occurs when initial exposure to an allergen leads to the production of allergen-specific IgE. The second, or effector phase, occurs when re-exposure to the same allergen triggers the activation of sensitized mast cells and the subsequent clinical reaction. Persistently elevated IgE levels are particularly observed in atopic individuals, including those with allergic rhinitis or asthma [5, 19].

In this context, allergen-specific immunotherapy, commonly referred to as allergy shots or allergy vaccines, has emerged as a therapeutic approach aimed at reducing sensitivity to allergenic substances. Treatment involves the progressive administration of doses of the allergen responsible for the symptoms, with the aim of promoting desensitization and restoring immune balance. The efficacy of immunotherapy depends on factors such as the degree of patient sensitization, the type of allergy involved, and the frequency of allergen exposure. This strategy has been effective in controlling chronic manifestations such as rhinitis, asthma, and allergic rhinoconjunctivitis, which are frequently associated with continuous exposure to environmental allergens, including mites, pollen, and fungi [6, 20].

In recent years, advances in biotechnology have enabled the development of biologic medications that act with high specificity on molecular targets involved in the immune response. These agents include vaccines and monoclonal antibodies of human or animal origin that are modified in the laboratory to act directly on endogenous molecules, such as pro-inflammatory cytokines (TNF-α, IL-1, and IL-6) or cell surface receptors (CD20 and CD4) [7]. In the context of allergic diseases, most currently approved biologic agents target the type 2 (Th2) inflammatory pathway. These include monoclonal antibodies directed against IL-5, IgE, IL-4, and IL-13, which are particularly indicated for severe cases or those refractory to conventional treatment [8].

According to the Brazilian Association of Allergy and Immunology (ASBAI), approximately 30% of the Brazilian population has some form of allergy. Given the increasing prevalence of allergic respiratory diseases and the evolution of therapeutic approaches, understanding and comparing the efficacy of the different available treatment modalities is essential. Allergen-specific immunotherapy and biologic agents represent promising strategies for managing persistent, moderate, or severe cases of allergic rhinitis and asthma, with a direct impact on quality of life and disease control. In this context, the present study aimed to conduct a literature review to evaluate the efficacy and safety of allergen-specific immunotherapy and biologic agents in the treatment of respiratory allergies.

Methods

Study Design: This study was designed as a literature review aimed at evaluating the efficacy and safety of allergen-specific immunotherapy, including allergy vaccines, and biologic agents in the treatment of respiratory allergies, such as asthma and allergic rhinitis.

Search Strategy and Study Selection: The literature search was conducted using the PubMed and SciELO databases with the following search terms: “immunotherapy for anti-allergy vaccines,” “respiratory allergies,” “allergens,” “asthma,” and “rhinitis.” Studies published in Portuguese or English between 2014 and 2024 were eligible for inclusion.

The selection process involved an initial screening of titles and abstracts, followed by full-text assessment of articles considered potentially eligible according to the inclusion criteria. The search and selection procedures were used to organize the literature reviewed; however, no formal assessment of the risk of bias of the included studies was conducted.

Inclusion Criteria: Original studies investigating the use of allergen-specific immunotherapy or biologic agents for the treatment of asthma and/or allergic rhinitis in humans were included. Eligible studies were required to report relevant qualitative or quantitative clinical data on the efficacy, safety, or other therapeutic outcomes of these interventions and to employ an appropriate methodological design, including clinical trials, cohort studies, case-control studies, or observational studies providing consistent data.

Exclusion Criteria: Review articles, editorials, letters to the editor, conference abstracts, and studies for which the full text was unavailable were excluded. Studies conducted exclusively in animal models or in vitro, as well as publications addressing non-respiratory clinical conditions, were also excluded. Duplicate records identified across databases and articles that did not fall within the scope of the review were likewise excluded.

Data Analysis and Interpretation: The findings of the selected studies were analyzed qualitatively and descriptively through a narrative synthesis. The evidence was organized into tables and discussed in terms of clinical efficacy, safety, therapeutic outcomes, and the applicability of allergen-specific immunotherapy and biologic agents in the treatment of respiratory allergies. No meta-analysis or quantitative statistical analysis was performed.

Ethical Considerations: This literature review involved neither primary data collection nor direct participation of human subjects. Accordingly, submission to and approval by a Research Ethics Committee were considered unnecessary, in accordance with the guidelines established by Resolution No. 510/2016 of the Brazilian National Health Council, which exempts research based exclusively on bibliographic sources from ethical review.

Results

The literature search and study-selection process is summarized in Figure 1. The flowchart presents the records reported at the search and selection stages in the source figure.

Following study selection and literature analysis, a table was developed to summarize the main information regarding the use of immunotherapy (Table 1) and biologic medications (Table 2) in the treatment of respiratory allergies. The interventions were categorized according to the number of included studies, allowing their representation in the current scientific literature to be assessed.

The synthesis of the 65 articles identified two major groups of therapeutic strategies: allergen immunotherapy (AIT) and biologic medications. Among AIT modalities, subcutaneous immunotherapy (SCIT), sublingual immunotherapy (SLIT), sublingual tablets, intralymphatic immunotherapy, intradermal immunotherapy, and preseasonal regimens were highlighted. Among biologic medications, the studies focused primarily on dupilumab, mepolizumab, omalizumab, and benralizumab.

SCIT was associated with reduced rhinitis symptoms, decreased medication use, and improved quality of life, as well as changes in IgG4 levels and inflammatory markers. More recent studies have also described clinical and immunomodulatory benefits in patients with rhinitis and asthma. SLIT, including tablets for house dust mites and pollen, was associated with improvements in symptoms and quality of life, with adverse events predominantly local and of mild to moderate severity. Follow-up studies also suggested that these benefits may persist after treatment discontinuation.

Among biologic medications, dupilumab was the most frequently represented agent in the synthesis. Studies reported improvements in symptoms, quality of life, olfactory function, and asthma control in patients with chronic rhinosinusitis with nasal polyps, as well as reductions in biomarkers associated with type 2 inflammation. Mepolizumab, which targets IL-5, demonstrated benefits in reducing eosinophilia, corticosteroid use, and disease severity in patients with eosinophilic phenotypes. Omalizumab, in turn, demonstrated benefits in allergic asthma and rhinitis in clinical and observational studies.

Adverse events varied according to the therapeutic modality. With AIT, local reactions and mild to moderate symptoms were the most frequently observed events, although systemic reactions may occur and warrant clinical monitoring. Among biologic medications, mild adverse events predominated, including injection-site reactions, headache, and nonspecific symptoms. However, the safety profile depends on the medication, the phenotype being treated, and the duration of follow-up.

Table 1. Analysis of data from review articles on immunotherapy for the treatment of respiratory allergies

Pharmacological Class and Therapies:	Number of articles addressing the therapy:	Observed results:	Adverse effects:
[27-34]Sublingual tablets (drops/tablets for mites, house dust mites, timothy grass, SQ grass, and extracts of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*)	8	Sublingual immunotherapy (SLIT) significantly improved asthma and rhinitis symptoms, lung function, and disease control, while reducing airway inflammation and medication use. Benefits were more evident after 24 months and persisted for up to 5 years, with good tolerability and a favorable safety profile, including in children.	Adverse effects of the tablets were predominantly mild to moderate, mainly oral itching, throat irritation, and oral swelling. Few patients discontinued treatment, and no cases of anaphylaxis or death were reported.
[35-44]Specific immunotherapy (house dust mites, *Lolium perenne* peptides, grass pollen, tree pollen, weed and flower pollen, fungi, and epithelia)	10	Specific immunotherapy significantly reduced allergic symptoms and medication use, improving quality of life and immune response. Patients reported high satisfaction, safety, and ease of use, with similar benefits across different methods after three years of treatment.	Adverse effects were predominantly mild to moderate, mainly oral itching, throat irritation, and oral swelling. Approximately 2.3% experienced serious events and 19% experienced bothersome but non-serious events. No systemic
[45-53]Subcutaneous immunotherapy (house dust mites, animal dander, flower pollen, wool, feathers, *Olea europaea*, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, fungi, and *Phoenix dactylifera* pollen)	9	Subcutaneous immunotherapy (SCIT) significantly reduced rhinitis symptoms, improved quality of life, decreased medication use, and reduced nasal eosinophilia. Immune markers improved and safety was good, with only 8 systemic reactions. High asthma remission rates and reduced IL-33 levels were also observed after treatment.	Adverse effects were predominantly mild to moderate and non-serious, including headache, respiratory infections, pharyngitis, and skin reactions. Only 11 systemic events related to immunotherapy were recorded, with no cases of anaphylaxis or death.
[54]Intradermal immunotherapy (house dust mites)	1	Intradermal immunotherapy (IDIT) significantly reduced allergic rhinitis symptoms in children, with improvement apparent in the first month. It also reduced skin reactivity and increased IgG4 levels, showing good tolerability	No adverse effects were reported.

		and a favorable clinical response.	
[55-57]Intralymphatic immunotherapy (birch pollen, grass, timothy grass, and intralymphatic immunotherapy placebo)	3	Intralymphatic immunotherapy (ILIT) significantly reduced symptoms and medication use and improved quality of life for up to two years. It also promoted favorable immunological changes, such as increased regulatory T cells, IFN-γ, and IL-10, and reduced IgE, suggesting a lasting effect and potential as an alternative to conventional immunotherapy.	Mild local pain was the most common adverse event.
[58-63]Sublingual immunotherapy (house dust mites, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and grass pollen)	6	SLIT significantly improved rhinitis and asthma symptoms and quality of life after three years. It also promoted favorable immunological changes, including increased IgG4 and reduced eosinophils and allergen-specific IgE. The 300-SRU dose showed greater efficacy, with musculin (MSC) emerging as a possible response biomarker.	Adverse effects were predominantly mild to moderate, mainly oral itching and swelling and abdominal pain. Local reactions occurred in approximately 29% of patients and gastrointestinal reactions in about 6%, with no serious events or anaphylaxis reported.
[64]Three injections of an aluminum hydroxide-adsorbed allergoid preparation containing six grass allergens	1	The accelerated high-dose regimen showed safety and tolerability similar to the standard regimen in children and adolescents and was feasible in patients with or without asthma. IgE profiles did not differ significantly between groups.	Systemic allergic reactions occurred in approximately 5% of patients.
[65]Preseasonal immunotherapy (grass pollen)	1	Preseasonal grass-pollen immunotherapy significantly increased specific IgE and IgG4 levels and improved quality of life. Benefits were similar in monosensitized and polysensitized patients.	Not specified.

Abbreviations: SLIT, sublingual immunotherapy; SCIT, subcutaneous immunotherapy; IDIT, intradermal immunotherapy; ILIT, intralymphatic immunotherapy; HDM, house dust mites; IgE, immunoglobulin E; IgG, immunoglobulin G; IgG4, immunoglobulin G subclass 4; sIgG, allergen-specific immunoglobulin G; sIgG4,

allergen-specific immunoglobulin G4; IL-2, interleukin 2; IL-10, interleukin 10; IL-33, interleukin 33; IFN-γ, interferon gamma; Th2, type 2 helper T lymphocytes; MSC, musculin; SRU, standardized reactivity unit; TNSS, total nasal symptom score; fVAS, facial visual analog scale; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; PEF, peak expiratory flow; Phl p, designation for *Phleum pratense* (timothy grass) allergen.

Source: Prepared by the authors.

Table 2. Analysis of data from review articles on biologic drugs for the treatment of respiratory allergies

Pharmacological Class and Therapies:	Number of articles addressing the therapy:	Observed results:	Adverse effects:
[1-2]Benralizumab	2	After one year of treatment, symptoms and quality of life improved significantly, with reductions in SNOT-22, NPS, and VAS scores and improved asthma control (ACT). Reductions in eosinophils and neutrophils in nasal cytology were also observed, indicating benefits for both severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps.	Regarding nasal polyps, only 1 patient (5.8%) required surgery after treatment with benralizumab.No other adverse effects were mentioned.
[3-17]Dupilumab	15	Dupilumab significantly improved nasal polyps, quality of life, sense of smell, and asthma control, with few adverse effects. NPS and SNOT-22 scores decreased, ACT and FEV1 increased, and eosinophils and inflammatory biomarkers—including IgE, IL-13, and eotaxins—decreased. It also reduced severe exacerbations, demonstrating efficacy and good tolerability in patients with chronic rhinosinusitis with nasal polyps.	Adverse events associated with dupilumab were predominantly mild, mainly pain or discomfort at the injection site. Asymptomatic hypereosinophilia, arthralgia, epiphora, and headache were also reported, with a decrease in event frequency and intensity over the course of treatment.
[18-21]Mepolizumab	4	Mepolizumab showed a 70% response rate in eosinophilic chronic rhinosinusitis, reducing symptoms, corticosteroid use, and FeNO. In patients with severe CRSwNP, it also reduced polyp size, nasal obstruction, and the need for surgery and systemic corticosteroids.	After eight months of mepolizumab treatment, one patient developed right-sided cervical lymphadenopathy.No other adverse effects were mentioned.
[22]Reslizumab	1	Reslizumab reduced peripheral eosinophil counts but did not improve sinonasal symptoms. The results suggest that eosinophils may not be the main mediators of the disease, whereas mast cells may play a relevant role in the persistence of symptoms.	Not specified.

[23-26]Omalizumab	4	Omalizumab significantly improved lung function, asthma control, nasal and ocular symptoms, and quality of life. Medication use, corticosteroid use, and FeNO decreased; benefits were also reported across different allergic diseases, including rhinitis, chronic urticaria, and atopic dermatitis.	Adverse effects of omalizumab were generally mild and infrequent, mainly injection-site reactions, headache, nausea, and fatigue. Only 3.5% of patients discontinued treatment because of adverse events, and no serious events were reported.

Abbreviations: ACT, Asthma Control Test; SNOT-22, 22-item Sino-Nasal Outcome Test; NPS, nasal polyp score; VAS, visual analog scale; CRSwNP, chronic rhinosinusitis with nasal polyps; FeNO, fractional exhaled nitric oxide; IL-13, interleukin 13; FEV1, forced expiratory volume in one second.

Source: Prepared by the authors.

Immunotherapies: Allergen immunotherapy, commonly referred to as allergy shots or allergy vaccines, represents a therapeutic approach aimed at reducing sensitivity in individuals who develop allergic reactions to specific substances [6].

The immunotherapy modalities identified in the results of the present study included sublingual tablets, allergen-specific immunotherapy, intradermal immunotherapy, intralymphatic immunotherapy, subcutaneous immunotherapy, a regimen consisting of three injections of an aluminum hydroxide-adsorbed allergoid preparation containing six grass species, and preseasonal immunotherapy. Notably, the most frequently identified approaches were allergen-specific immunotherapy (10 articles), subcutaneous immunotherapy (9 articles), sublingual tablets (8 articles), and sublingual immunotherapy (6 articles). These findings indicate the predominance of these immunotherapy modalities in clinical practice and underscore their relevance.

However, it is important to note that allergen-specific immunotherapy, which was extensively documented in the results of this study, involves a variety of allergens, including house dust mites, Lolium perenne peptides, grass, tree, and weed pollens, flowers, fungi, and epithelial allergens. This approach involves administering a vaccine containing the allergens responsible for the allergic reaction, with the aim of enhancing the patient's immune response and reducing sensitivity to a specific substance [20].

Allergen-specific immunotherapy is recommended when patients cannot avoid allergen exposure or when pharmacological treatment does not provide a satisfactory response. This treatment is effective in preventing IgE-mediated allergic diseases in atopic individuals by reducing the degree of sensitization, as reflected by IgE antibody levels, and tissue responses to allergens, thereby preventing severe immediate allergic reactions. Furthermore, this therapy may modify the underlying features of chronic allergic conditions, making it particularly relevant to the management of rhinitis and asthma. It is also indicated for patients who experience anaphylaxis following insect stings. The approach is based on the

administration of multiple doses of allergen extracts at gradually increasing concentrations and at regular intervals over a period that may range from one to five years. The objective is to achieve clinical tolerance in hypersensitive patients, thereby attenuating symptoms following exposure to specific allergens [9].

In the present study, significant positive outcomes were observed, including relevant changes in allergic symptoms, improvements in patients' quality of life, and reductions in the severity of clinical manifestations. The efficacy of immunotherapy was supported by changes in skin test responses and decreased use of antiallergic medications. Treated patients exhibited lower allergen reactivity and reduced levels of inflammatory mediators, suggesting a more effective immune response. Furthermore, most participants reported that the treatment was safe and easily incorporated into their daily routines, indicating high levels of satisfaction with the treatment process.

Previous studies, including those by [10, 11], support these findings, demonstrating that immunotherapy not only improves allergic symptoms but also reduces long-term dependence on medication. These studies further reported that, after three years of treatment, immunotherapy efficacy was comparable across different modalities, with no significant differences in safety outcomes. Thus, the literature highlights the importance and efficacy of immunotherapy in the management of allergic diseases [10, 11].

Regarding subcutaneous immunotherapy (SCIT), the treatments included allergens such as house dust mites, animal dander, flower pollens, wool, feathers, Olea europaea, Dermatophagoides pteronyssinus, Dermatophagoides farinae, Blomia tropicalis, fungi, and Phoenix dactylifera pollen. It is important to emphasize that allergen immunotherapy is predominantly administered through subcutaneous injections, in which progressively increasing doses of the allergen responsible for sensitization are administered until a maintenance dose is reached. Treatment duration generally ranges from approximately 3 to 5 years after the maximum clinical effect has been achieved, with this decision influenced by individual factors that may affect the patient's response. Although immunotherapy aims to modulate the immune response and reduce sensitivity to specific allergens, continuous monitoring of treatment progress and patient response is essential to ensure the safety and efficacy of the procedure [20].

The SCIT findings demonstrated a significant improvement in allergic rhinitis symptoms, with an approximately 79% mean reduction in symptom scores at the end of treatment. Patients experienced improvements in symptoms such as nasal itching, sneezing, and congestion, resulting in a better quality of life. Regarding immunological parameters, significant increases in sIgG and sIgG4 levels were reported, along with reduced allergen-specific reactivity. After three months of treatment, a decrease in medication use and improvements in clinical biomarkers, including interleukin-33, were observed. SCIT also demonstrated efficacy in reducing nasal eosinophilia and improving allergen provocation test results. These findings suggest that SCIT is not only safe and effective but may also contribute to asthma remission over time (Table 1).

Furthermore, sublingual tablets are medications placed under the tongue, where they dissolve in saliva. The main advantage of this route of administration is the direct absorption of the medication into the systemic circulation, thereby avoiding first-pass hepatic metabolism [12]. In the articles analyzed in this study, these tablets contained various allergens, including anti-mite drops, house dust mites, Timothy grass, SQ grass, and extracts of Dermatophagoides pteronyssinus and Dermatophagoides farinae.

The findings concerning sublingual tablets indicated significant improvements in asthma and rhinitis symptoms. Studies demonstrated reductions in both daytime and nighttime symptoms, together with improvements in pulmonary function parameters, including forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and peak expiratory flow (PEF), as well as better disease control, particularly after 24 months of treatment. In addition, these treatments were associated with reduced eosinophil counts and decreased airway wall thickness. Quality of life improved, with reductions in rhinitis and asthma symptoms and decreased medication use. Grass pollen and house dust mite sublingual tablets demonstrated efficacy in reducing asthma and rhinoconjunctivitis symptoms, with a favorable safety profile, including in children. Positive effects were reported for up to five years after treatment initiation, suggesting sustained benefits (Table 1).

Finally, it is important to emphasize that the sublingual immunotherapy (SLIT) formulations described in this study included a variety of allergens, namely house dust mites, Dermatophagoides pteronyssinus, Dermatophagoides farinae, and grass pollens. In this treatment modality, the allergen responsible for the allergic reaction is administered in progressively increasing doses, using drops placed under the tongue daily or three times per week. Treatment duration varies according to individual patient characteristics and generally ranges from 3 to 5 years. Moreover, because administration is sublingual, patients can administer the treatment at home, avoiding needle-related discomfort and the need for weekly visits to a healthcare facility for injections [13].

In the studies analyzed, SLIT demonstrated consistent results in the treatment of allergic rhinitis, with significant improvements in symptoms and quality of life after three years of follow-up. The therapy stimulated the expansion of Th2 and regulatory T cells while reducing the reactivity of functional Th2 cells, indicating a beneficial immunological effect. Among treated patients, reductions in symptom scores related to asthma and rhinitis were observed. Analysis of immunological biomarkers further supported these findings, highlighting increased expression of musculin (MSC) in pathogenic Th2 cells, associated with their differentiation into regulatory T cells; reduced serum eosinophil counts; increased IgG4 levels and IgE-blocking activity; and a progressive decrease in allergen-specific IgE. These findings indicated a dose-dependent response, with a dose of 300 standardized reactivity units (SRU) considered the most effective. Finally, quality-of-life assessments revealed substantial improvements in daily activities, sleep quality, and allergic symptoms (Table 1).

Regarding subcutaneous and sublingual immunotherapy, it is important to emphasize that sublingual allergen preparations, available as drops or tablets, are reported to be as effective as injectable formulations and to have a more favorable safety profile, with fewer adverse reactions. These

preparations are indicated for the treatment of asthma, allergic rhinitis, and atopic dermatitis and offer the advantage of home administration, eliminating the need for frequent clinic visits required for injectable treatment. Furthermore, they are effective in treating allergies to pollen and house dust mites when administered at sufficiently high doses of standardized allergens [6]. Studies indicate that both routes are highly effective and may induce remission of allergic diseases, particularly rhinitis and asthma, with symptom control lasting approximately 10 years after treatment discontinuation [6].

Regarding adverse events associated with immunotherapy, allergen-specific immunotherapy was reported to have the most severe adverse events, with approximately 2.3% of patients experiencing severe reactions, including angioedema of the tongue and lips, post-bronchoscopy pleuritis, and pyelonephritis. The other modalities—SCIT, sublingual tablets, and SLIT—were associated with mild to moderate adverse events, including headache, upper respiratory tract infections, pharyngitis, oral pruritus, oral edema, and abdominal pain.

Biologic Medications: The concept of biologic medications encompasses vaccines and laboratory-modified antibodies of human or animal origin that act directly on specific endogenous molecules [7].

In this study, the biologic medications benralizumab, dupilumab, mepolizumab, omalizumab, and reslizumab were analyzed. These therapies have received approval from the Brazilian Health Regulatory Agency (ANVISA) and the US Food and Drug Administration (FDA) for clinical use in specific conditions, following rigorous clinical studies demonstrating their efficacy and safety for indications such as asthma and rhinitis. However, further research and clinical trials are ongoing to evaluate the efficacy of these medications in other diseases and explore new indications or therapeutic combinations [17].

Dupilumab was the most frequently mentioned and utilized medication in the collected data, being referenced in 15 of the selected articles. Mepolizumab and omalizumab ranked next, each being cited in four articles.

It is important to emphasize that dupilumab is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4 receptor alpha (IL-4Rα) subunit, which is shared by the receptor complexes for IL-4 and IL-13. Dupilumab inhibits IL-4 signaling through the type 1 receptor and both IL-4 and IL-13 signaling through the type 2 receptor. By blocking the IL-4Rα subunit, dupilumab inhibits responses induced by IL-4 and IL-13, including the release of pro-inflammatory cytokines, chemokines, and immunoglobulin E (IgE) [3].

According to [14], this type of immune response is mediated by T helper 2 (Th2) lymphocytes, cells of the adaptive immune system that play an essential role in defense against extracellular parasites and in allergic responses. Th2-mediated inflammation is associated with allergic diseases, such as asthma, allergic rhinitis, and atopic dermatitis, as well as with certain autoimmune diseases. By blocking these pathways, dupilumab helps reduce inflammation, hypersensitivity, and symptoms associated with allergic and inflammatory diseases [8].

In the data collected for this study, dupilumab was used predominantly to treat chronic rhinosinusitis with nasal polyps, resulting in improvements in quality of life, olfactory function, and asthma control, with a low incidence of adverse effects. Injection-site discomfort was the most commonly reported complaint. The results showed that, after two months of treatment, symptoms decreased significantly, with a two-point reduction in the nasal polyp score (NPS) and a 42-point reduction in the 22-item Sino-Nasal Outcome Test (SNOT-22). Improvements continued over time, although they became less pronounced. Furthermore, treatment led to a significant reduction in eosinophil counts and decreases in inflammatory biomarkers, including eosinophil cationic protein ($P = 0.008$), eotaxin-2 ($P = 0.008$), eotaxin-3 ($P = 0.031$), IgE ($P = 0.023$), and IL-13 ($P = 0.031$), suggesting that nasal cytology may be a promising method for monitoring treatment response (Table 2). These findings are consistent with the literature reported by Wollenberg and colleagues, which highlights the efficacy of dupilumab not only in reducing symptoms but also in modulating the underlying inflammatory response, reinforcing its role as an innovative therapeutic option for chronic conditions such as rhinosinusitis [15].

In contrast, mepolizumab, a humanized monoclonal antibody targeting interleukin-5 (IL-5), acts through a different mechanism by focusing on eosinophil regulation. IL-5 is essential for the growth and survival of these leukocytes, and by inhibiting its bioactivity, mepolizumab reduces eosinophil production and activity [16]. In the present study, treatment with mepolizumab yielded a response rate of 70% in patients with eosinophilic chronic rhinosinusitis, resulting in significant improvements in systemic corticosteroid use, fractional exhaled nitric oxide (FeNO) levels, and symptom severity. It is worth noting that, although the treatment was generally well tolerated, one patient developed cervical lymphadenopathy after eight months of treatment, while no other adverse events were reported (Table 2).

Omalizumab, another humanized monoclonal antibody, acts through a distinct mechanism by binding to circulating immunoglobulin E (IgE) and preventing its interaction with the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. This action reduces circulating IgE levels and inhibits cellular activation, which is essential to the cascade of chemical mediator release involved in allergic responses [17]. The findings of the present study demonstrated significant improvements in pulmonary function, asthma control, and patients' quality of life, as well as an increase in quality-adjusted life-years. Visual analog scale (VAS) scores indicated significant reductions in symptoms such as nasal obstruction and rhinorrhea, with 73% of patients reducing or discontinuing the use of symptomatic medications. Preseasonal administration of omalizumab also resulted in a significant reduction in nasal symptoms during the pollen season, leading to a greater number of days without the need for medication (Table 2).

Regarding adverse events, dupilumab, mepolizumab, and omalizumab exhibited favorable safety profiles, with events generally being mild and infrequent. For dupilumab, the reported adverse events were predominantly mild, with injection-site discomfort being the most common complaint. During follow-up, 24 patients reported adverse reactions, including injection-site pain, asymptomatic hypereosinophilia, arthralgia, epiphora, and headache. The frequency and intensity of these events decreased over the course of treatment. With omalizumab, patients reported local reactions, such as itching and swelling at

the injection site, which resolved rapidly. After 4 and 12 months of therapy, the most common adverse events included headache, nausea, dysphonia, and fatigue. Mepolizumab exhibited a similar safety profile, but with a lower incidence of serious adverse events; only one case of cervical lymphadenopathy was reported after eight months of treatment.

These comparisons highlight not only the differences in the mechanisms of action of the three medications but also the diversity of the observed clinical responses. Whereas dupilumab appears effective in modulating inflammatory responses and improving quality of life, mepolizumab and omalizumab demonstrate particular relevance in the contexts of eosinophilia and IgE-mediated hypersensitivity, respectively. Treatment selection should therefore take into account patients' clinical characteristics and their individual responses to each therapy (Table 2).

Furthermore, regarding biologic medications, it is important to note that benralizumab and reslizumab were also identified in the study results. However, their occurrence was limited, and the available findings were insufficiently substantial to warrant further discussion in the present review.

Immunotherapy or Biologic Agents: It is essential to distinguish allergen immunotherapy from biologic agents. The main difference is that allergen immunotherapy promotes immunological tolerance to specific allergens, whereas biologic agents block signaling pathways involved in immune responses, modifying how the body responds to allergens and thereby reducing allergic reactions [18].

Allergen immunotherapy was introduced in 1911 by Noon and Freeman. However, it has gained increasing attention in recent years due to the rising prevalence of allergic diseases and its role as a therapeutic option for asthma, rhinitis, and atopic dermatitis. It involves the gradual administration of increasing doses of the allergen responsible for the allergic reaction, with the aim of desensitizing the immune system and reducing the allergic response [6].

In contrast, biologic agents are medications administered primarily by injection, although some biologic products can be administered through other routes, that act directly on cells and molecules involved in allergic reactions [18]. Nevertheless, based on the findings of the present study, a comparative analysis of biologic medications and allergen immunotherapy indicates that both approaches are effective, although each offers specific advantages depending on patient characteristics and treatment objectives.

Biologic agents demonstrated significant efficacy in asthma and chronic rhinosinusitis with nasal polyps (CRSwNP), improving quality of life and reducing eosinophil and neutrophil levels. Furthermore, dupilumab, benralizumab, mepolizumab, and omalizumab were associated with consistent reductions in inflammatory biomarkers, including eosinophil cationic protein, eotaxin-2, eotaxin-3, total IgE, allergen-specific IgE, and IL-13, alongside improvements in pulmonary function and clinical symptom control. Based on the findings of the present study, these agents are particularly relevant for severe eosinophilic asthma and allergic conditions accompanied by comorbidities. Their favorable clinical responses may also contribute to treatment adherence.

Regarding allergen immunotherapy, SCIT and SLIT demonstrated significant improvements in rhinitis and asthma symptoms, with SCIT achieving a cumulative remission rate of 86.9%. SLIT stood out for its safety profile and ease of administration, particularly in children, and demonstrated efficacy against specific allergens, such as pollen and house dust mites. In addition to alleviating symptoms, allergen immunotherapy promotes long-lasting immunomodulation, with benefits that may persist for years after treatment discontinuation, improving quality of life and reducing medication use.

With respect to adverse events, allergen immunotherapy generally presented a higher frequency of local and systemic reactions of mild to moderate severity, such as oral pruritus and edema, with approximately 5% of patients receiving SLIT reporting systemic reactions. Biologic agents, in contrast, were associated with fewer serious adverse events and lower treatment discontinuation rates, with mild injection-site reactions among the most commonly reported events.

In summary, biologic agents appear particularly beneficial in severe and complex allergic diseases accompanied by comorbidities, whereas allergen immunotherapy offers long-term benefits and is especially relevant for the prevention and control of common allergic symptoms, with a favorable safety profile. Although allergen immunotherapy may require several months to produce clinically significant results, biologic agents may act more rapidly, providing symptom relief within a shorter period. Both therapeutic approaches may be effective, and treatment selection should depend on patient characteristics and the desired immunological response [18].

Discussion

The findings of this review indicated that allergen immunotherapy (AIT) and biologic medications act at distinct points in the pathophysiology of respiratory allergies. AIT is characterized by controlled allergen exposure and the progressive induction of tolerance mechanisms, whereas biologic medications block specific targets involved in the inflammatory response [4,6]

The evidence gathered for subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) was consistent with clinical benefits in allergic rhinitis, particularly in terms of symptom reduction and decreased medication use. Recent studies have also demonstrated changes in IgG4, allergen-specific IgE, and regulatory cells, suggesting that the effects extend beyond symptom control [7,14,23,27,28]. However, treatment responses varied according to the allergen, the product used, the route of administration, and patient characteristics, precluding the generalization of results obtained with one preparation to all forms of AIT.

Within the group of biologic medications, the findings were more directly associated with the inflammatory phenotype. By blocking IL-4 and IL-13 signaling, dupilumab demonstrated favorable outcomes in chronic rhinosinusitis with nasal polyps and conditions associated with type 2 inflammation [15, 17, 24, 26]. Mepolizumab targets the IL-5 pathway and demonstrated benefits particularly related to eosinophilic disease [18, 19, 29]. Omalizumab, which targets IgE, showed favorable outcomes in

selected allergic diseases [20,22, 26]. These findings reinforce that the outcomes of biologic medications should not be considered equivalent across different molecules or clinical phenotypes.

Safety must also be interpreted according to the therapeutic strategy. SLIT tends to be associated with local adverse events, whereas SCIT requires attention to the possibility of systemic reactions. Among biologic medications, the adverse events reported in the selected studies were predominantly mild; however, treatment duration and the characteristics of the study populations influenced safety assessments [8, 9, 11, 18, 20, 22, 26, 29].

One limitation of this review was the heterogeneity of the studies regarding populations, allergens, products, routes of administration, outcomes, and follow-up duration. In addition, no formal assessment of the risk of bias of the included studies was conducted, and no quantitative estimation of intervention effects was performed. Therefore, the findings should be interpreted as a descriptive synthesis of the selected literature, and the possibility that methodological limitations in the included studies influenced the results cannot be excluded.

Conclusion

The literature analyzed indicated that AIT and biologic medications provide benefits in the management of respiratory allergies, although they differ in their mechanisms of action, indications, and safety profiles. SCIT and SLIT demonstrated benefits primarily in symptom control and modulation of the immune response, whereas biologic medications showed clinically relevant outcomes in specific phenotypes, particularly in severe disease and type 2 inflammation. Treatment selection should be individualized and based on clinical phenotype, sensitization, disease severity, previous treatment response, safety, adherence, and patient characteristics [26, 29]. The findings provide a comprehensive overview of the efficacy of these therapies, considering aspects such as symptom reduction, inflammation control, and improvements in patients' quality of life. Furthermore, data on adverse events are essential for understanding the challenges associated with the long-term use of these therapeutic approaches, contributing to a critical assessment of the risk–benefit profile of each treatment.

Declarations

Author contributions:

Anna Karolina Andrade Moura: Contributed substantially to the conception and development of the study, data acquisition, analysis and interpretation, and the original drafting of the manuscript. She approved the final version for publication and agrees to be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Mariana de Almeida Azevedo: Contributed to the scientific supervision of the study, its conception, and the critical review of its intellectual content. She approved the final version for publication and agrees to

be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Luciana de Andrade Agostinho: Contributed to the critical review and rewriting of the manuscript to adapt it for scientific publication. She approved the final version for publication and agrees to be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Igor Vilaça Lima Romano: Contributed to the critical review and rewriting of the manuscript, as well as its translation into English for scientific publication. He approved the final version for publication and agrees to be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

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Ethics statement: This is a literature review based exclusively on published literature, with no primary data collection or direct involvement of human participants; therefore, submission to a Research Ethics Committee was not required.

References

1. ABBAS, Abul K.; LICHTMAN, Andrew H.; PILLAI, Shiv. Imunologia Básica: funções e distúrbios do sistema imunológico. Rio de Janeiro: Grupo GEN, 2021.
2. MORAES, Sandra do L.; FERREIRA, Antonio W. Diagnóstico Laboratorial das Principais Doenças Infecciosas e Autoimunes. 3. ed. Rio de Janeiro: Grupo GEN, 2013.
3. ABBAS, Abul K.; LICHTMAN, Andrew H.; PILLAI, Shiv. Imunologia Celular e Molecular. 10. ed. Rio de Janeiro: GEN Guanabara Koogan, 2023.
4. SILVA, Lucienir M.; ROSELINO, Ana Maria F. Reações de hipersensibilidade a drogas (farmacodermia). Revista Medicina, v. 36, p. 460-471, abr./dez. 2003.
5. KASHIWABARA, Tatiliana Bacelar et al. Medicina ambulatorial V com ênfase em alergia e imunologia. Montes Claros, MG: Dejan Gráfica e Editora, 2018.
6. ASBAI. Imunoterapia com Alérgenos. 2018.
7. PRADO, Mônica Simon; ROCHA, Sara de Brito; ANDRADE, Luis Eduardo Coelho. Imunogenicidade dos fármacos imunobiológicos. Revista Paulista de Reumatologia, v. 15, n. 3, jul./set. 2016.
8. FRANZESE, Christine B. et al. Alergia em Otorrinolaringologia. Rio de Janeiro: Thieme Revinter, 2020.
9. ROSA, Tamine Jandrey da. Imunoterapia específica para o tratamento de alergias respiratórias: uma revisão sobre seu uso. Revista RBAC, abr. 2016.
10. PASSALACQUA, G. et al. MACVIA-ARIA Sentinel Network for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. Allergy, v. 70, n. 11, p. 1372-1392, 2015.

11. DURHAM, S. R. et al. Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: an EAACI Position Paper. Allergy, v. 69, n. 7, p. 854-867, 2014.
12. LUIZ, Regis. Farmacotécnica de Comprimidos Sublinguais: Um Guia para Farmacêuticos Magistrais. Pharmaceutical Consultoria, 16 maio 2024.
13. CENTRO DE RINITE E ALERGIA. Vacina para rinite: como funciona a Imunoterapia? 31 mar. 2023.
14. ATHANAZIO, Rodrigo. Já ouviu falar em inflamação Th2? Tema importante para portadores de doenças respiratórias? Clínica de doenças respiratórias avançadas, 31 jul. 2024.
15. WOLLENBERG, A. et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. Journal of the European Academy of Dermatology and Venereology, v. 32, n. 5, p. 657-682, 2018.
16. NUCALA. Modelo de texto de bula – Paciente. Glaxo Operations UK Ltd., ANVISA, 2020.
17. AZEREDO, Flaubertt Santana de. Omalizumabe. Secretaria de Saúde do Distrito Federal, 2021.
18. ALERGOCLÍNICA. Imunobiológicos: o que são e qual a diferença para imunoterapia. 17 jul. 2023.
19. ABBAS, A. K.; LICHTMAN, A. H.; PILLAI, S. Imunologia celular e molecular. 7. ed. Rio de Janeiro: Elsevier, 2012.
20. ABBAS, Malak; MOUSSA, Mohamed; AKEL, Hassan. Type I Hypersensitivity Reaction. 17 jul. 2023. Disponível em: https://www.ncbi.nlm.nih.gov/books/NBK560561/. Acesso em: 3 mar. 2024.
21. AH LBECK, L. et al. Intralymphatic immunotherapy with one or two allergens renders similar clinical response in patients with allergic rhinitis due to birch and grass pollen. Clinical & Experimental Allergy, v. 52, n. 6, p. 747-759, 2022. doi: 10.1111/cea.14138.
22. AH LBECK, L. et al. Intralymphatic immunotherapy with birch and grass pollen extracts: a randomized double-blind placebo-controlled clinical trial. Clinical & Experimental Allergy, v. 53, n. 8, p. 809-820, 2023. doi: 10.1111/cea.14307.
23. CORREN, J. et al. Short-Term Subcutaneous Allergy Immunotherapy and Dupilumab are Well Tolerated in Allergic Rhinitis: A Randomized Trial. Journal of Asthma and Allergy, v. 14, p. 1045-1063, 2021. doi: 10.2147/JAA.S318892.
24. DEMOLY, P. et al. A 300 IR sublingual tablet is an effective, safe treatment for house dust mite-induced allergic rhinitis: an international, double-blind, placebo-controlled, randomized phase III clinical trial. Journal of Allergy and Clinical Immunology, v. 147, n. 3, p. 1020-1030.e10, 2021. doi: 10.1016/j.jaci.2020.07.036.
25. DEMOLY, P. et al. Effective treatment of house dust mite-induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: results from a randomized, double-blind, placebo-controlled phase III trial. Journal of Allergy and Clinical Immunology, v. 137, n. 2, p. 444-451.e8, 2016. doi: 10.1016/j.jaci.2015.06.036.
26. JONSTAM, K. et al. Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. Allergy, v. 74, n. 4, p. 743-752, 2019. doi: 10.1111/all.13685.

27. NUMATA, T. et al. Efficacy of mepolizumab for patients with severe asthma and eosinophilic chronic rhinosinusitis. BMC Pulmonary Medicine, v. 19, n. 1, art. 176, 2019. doi: 10.1186/s12890-019-0952-1.
28. MASIERI, S. et al. Effects of omalizumab therapy on allergic rhinitis: a pilot study. European Review for Medical and Pharmacological Sciences, v. 20, n. 24, p. 5249-5255, 2016.
29. ZHANG, Y. et al. Omalizumab is effective in the preseasonal treatment of seasonal allergic rhinitis. Clinical and Translational Allergy, v. 12, n. 1, e12094, 2022. doi: 10.1002/clt2.12094.

References tables:

1. Cavaliere C, Segatto M, Ciofalo A, Colizza A, Minni A, Messineo D, Lambiase A, Greco A, de Vincentiis M, Masieri S. Benralizumab reduces eosinophils and inflammatory markers in patients with severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: A pilot real-life study. Immunol Lett. 2022 Aug;248:70-77. doi: 10.1016/j.imlet.2022.06.009. Epub 2022 Jun 23. PMID: 35752279.
2. Santomasi C, Buonamico E, Dragonieri S, Iannuzzi L, Portacci A, Quaranta N, Carpagnano GE. Effects of benralizumab in a population of patients affected by severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: a real life study. Acta Biomed. 2023 Feb 13;94(1):e2023028. doi: 10.23750/abm.v94i1.13474. PMID: 36786266; PMCID: PMC9987478.
3. Trimarchi M, Vinciguerra A, Rampi A, Tanzini U, Nonis A, Yacoub MR, Bussi M. A prospective study on the efficacy of dupilumab in chronic rhinosinusitis with type 2 inflammation. Acta Otorhinolaryngol Ital. 2022 Dec;42(6):538-544. doi: 10.14639/0392-100X-N2156. PMID: 36654520; PMCID: PMC9853107.
4. Al-Ahmad M, Ali A, Khalaf M, Alterki A, Rodriguez-Bouza T. Comorbid asthma in patients with chronic rhinosinusitis with nasal polyps: did dupilumab make a 63 difference? BMC Pulm Med. 2023 Jul 18;23(1):266. doi: 10.1186/s12890-023-02556 8. PMID: 37464395; PMCID: PMC10354942. Alergoclínica. Imunobiológicos: o que são e qual a diferença para imunoterapia. 17
5. Danisman Z, Linxweiler M, Kühn JP, Linxweiler B, Solomayer EF, Wagner M, Wagenpfeil G, Schick B, Berndt S. Differential nasal swab cytology represents a valuable tool for therapy monitoring but not prediction of therapy response in chronic rhinosinusitis with nasal polyps treated with Dupilumab. Front Immunol. 2023 Apr 18;14:1127576. doi: 10.3389/fimmu.2023.1127576. PMID: 37180133; PMCID: PMC10173305.
6. Maspero JF, Katelaris CH, Busse WW, Castro M, Corren J, Chipps BE, Peters AT, Pavord ID, Ford LB, Sher L, Rabe KF, Rice MS, Rowe P, Lu Y, Harel S, Jagerschmidt A, Khan AH, Kamat S, Pirozzi G, Amin N, Ruddy M, Graham NMH, Mannent LP, Teper A. Dupilumab Efficacy in Uncontrolled, Moderate-to-Severe Asthma with Self-Reported Chronic Rhinosinusitis. J Allergy Clin Immunol Pract. 2020 Feb;8(2):527-539.e9. doi: 10.1016/j.jaip.2019.07.016. Epub 2019 Jul 24. PMID: 31351189.
7. Bachert C, Hellings PW, Mullol J, Naclerio RM, Chao J, Amin N, Grabher A, Swanson BN, Hamilton JD, Guillonneau S, Taniou C, Zhang D, Pirozzi G, Graham NMH, Staudinger H, Mannent LP, Khan A. Dupilumab improves patient-reported outcomes in patients with chronic rhinosinusitis with nasal

polyps and comorbid asthma. J Allergy Clin Immunol Pract. 2019 Sep-Oct;7(7):2447-2449.e2. doi: 10.1016/j.jaip.2019.03.023. Epub 2019 Mar 27. PMID: 30928658.

8. Galletti C, Ragusa M, Sireci F, Ciodaro F, Barbieri MA, Giunta G, Grigaliute E, Immordino A, Lorusso F, Dispenza F, Freni F, Galletti F, Gallina S, La Mantia I, Galletti B. Dupilumab in chronic rhinosinusitis with nasal polyps: Real life data in a multicentric Sicilian experience. Am J Otolaryngol. 2024 Jan-Feb;45(1):104106. doi: 10.1016/j.amjoto.2023.104106. Epub 2023 Nov 5. PMID: 37948824.
9. Jonstam K, Swanson BN, Mannent LP, Cardell LO, Tian N, Wang Y, Zhang D, Fan C, Holtappels G, Hamilton JD, Grabher A, Graham NMH, Pirozzi G, Bachert C. 73 Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. Allergy. 2019 Apr;74(4):743-752. doi: 10.1111/all.13685. Epub 2019 Jan 21. PMID: 30488542; PMCID: PMC6590149.
10. Hopkins C, Wagenmann M, Bachert C, Desrosiers M, Han JK, Hellings PW, Lee SE, Msihid J, Radwan A, Rowe P, Amin N, Deniz Y, Ortiz B, Mannent LP, Rout R. Efficacy of dupilumab in patients with a history of prior sinus surgery for chronic 72 rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol. 2021 Jul;11(7):1087 1101. doi: 10.1002/alr.22780. Epub 2021 Feb 21. PMID: 33611847; PMCID: PMC8359289. Hoshino M, Akitsu K, Kubota K, Ohtawa J. Efficacy of a
11. Peters AT, Soler ZM, Kern RC, Heffler E, Maspero JF, Crampette L, Fujieda S, Lane AP, Zhang H, Nash S, Khan AH, Siddiqui S, Jacob-Nara JA, Rowe P, Deniz Y. Improvement in patient-reported "taste" and association with smell in dupilumab-treated patients with severe chronic rhinosinusitis with nasal polyps from the SINUS-24 and SINUS-52 trials. Clin Exp Allergy. 2022 Sep;52(9):1105 1109. doi: 10.1111/cea.14194. Epub 2022 Jul 12. PMID: 35775319; PMCID: PMC9545952.
12. Kamal MA, Franchetti Y, Lai CH, Xu C, Wang CQ, Radin AR, O'Brien MP, Ruddy M, Davis JD. Pharmacokinetics and Concentration-Response of Dupilumab in Patients With Seasonal Allergic Rhinitis. J Clin Pharmacol. 2022 May;62(5):689 695. doi: 10.1002/jcph.2004. Epub 2022 Jan 6. PMID: 34791679; PMCID: PMC9303412.
13. Pelaia C, Benfante A, Busceti MT, Caiaffa MF, Campisi R, Carpagnano GE, Crimi N, D'Amato M, Foschino Barbaro MP, Maglio A, Minenna E, Nolasco S, Paglino G, Papia F, Pelaia G, Portacci A, Ricciardi L, Scichilone N, Scioscia G, Triggiani M, Valenti G, Vatrella A, Crimi C. Real-life effects of dupilumab in patients with severe type 2 asthma, according to atopic trait and presence of chronic rhinosinusitis with nasal polyps. Front Immunol. 2023 Mar 30;14:1121237. doi: 10.3389/fimmu.2023.1121237. PMID: 37063895; PMCID: PMC10098307.
14. van der Lans RJL, Fokkens WJ, Adriaensen GFJPM, Hoven DR, Drubbel JJ, Reitsma S. Real-life observational cohort verifies high efficacy of dupilumab for chronic rhinosinusitis with nasal polyps. Allergy. 2022 Feb;77(2):670-674. doi: 10.1111/all.15134. Epub 2021 Oct 18. PMID: 34626497; PMCID: PMC9298295.
15. Hardison SA, Senior BA. The argument against the use of dupilumab in patients with limited polyp burden in chronic rhinosinusitis with nasal polyposis (CRSwNP). J Otolaryngol Head Neck Surg. 2023 Sep 28;52(1):64. doi: 10.1186/s40463-023-00668-z. PMID: 37759322; PMCID: PMC10537999.

16. Fujieda S, Matsune S, Takeno S, Asako M, Takeuchi M, Fujita H, Takahashi Y, Amin N, Deniz Y, Rowe P, Mannent L. The Effect of Dupilumab on Intractable Chronic Rhinosinusitis with Nasal Polyps in Japan. Laryngoscope. 2021 Jun;131(6):E1770-E1777. doi: 10.1002/lary.29230. Epub 2020 Nov 23. PMID: 33226139; PMCID: PMC8247406.
17. Paoletti G, Casini M, Malvezzi L, Pirola F, Russo E, Nappi E, Muci GQ, Montagna C, Messina MR, Ferri S, Racca F, Lamacchia D, Cataldo G, Puggioni F, De Virgilio A, Ferreli F, Mercante G, Spriano G, Canonica GW, Heffler E. Very Rapid Improvement in Extended Nitric Oxide Parameters Is Associated With Clinical and Functional Improvement in Patients With Chronic Rhinosinusitis With Nasal Polyps Treated With Dupilumab. J Investig Allergol Clin Immunol. 2023 Dec;33(6):457-463. doi: 10.18176/jiaci.0851. Epub 2022 Sep 1. PMID: 38095494.
18. Numata T, Nakayama K, Utsumi H, Kobayashi K, Yanagisawa H, Hashimoto M, Minagawa S, Ishikawa T, Hara H, Araya J, Kuwano K. Efficacy of mepolizumab for patients with severe asthma and eosinophilic chronic rhinosinusitis. BMC Pulm Med. 2019 Oct 12;19(1):176. doi: 10.1186/s12890-019-0952-1. PMID: 31606052; PMCID: PMC6790020.
19. Ho J, Walter S, Harvey RJ. Eosinophilic chronic rhinosinusitis and concurrent Kimura's disease treated with mepolizumab. BMJ Case Rep. 2021 Jan 18;14(1):e232627. doi: 10.1136/bcr-2019-232627. PMID: 33461987; PMCID: PMC7813409.
20. Fokkens W, Trigg A, Lee SE, Chan RH, Diamant Z, Hopkins C, Howarth P, Lund V, Mayer B, Sousa AR, Yancey S, Tabberer M; SYNAPSE study group. Mepolizumab improvements in health-related quality of life and disease symptoms in a patient population with very severe chronic rhinosinusitis with nasal polyps: psychometric and efficacy analyses from the SYNAPSE study. J Patient Rep Outcomes. 2023 Jan 20;7(1):4. doi: 10.1186/s41687-023-00543-5. PMID: 36662344; PMCID: PMC9859976.
21. Chupp G, Alobid I, Lugogo NL, Kariyawasam HH, Bourdin A, Chaker AM, Smith SG, Sousa AR, Mayer B, Chan RH, Matucci A. Mepolizumab Reduces Systemic Corticosteroid Use in Chronic Rhinosinusitis With Nasal Polyps. J Allergy Clin Immunol Pract. 2023 Nov;11(11):3504-3512.e2. doi: 10.1016/j.jaip.2023.08.015. Epub 2023 Aug 14. PMID: 37586475.
22. Staudacher AG, Peters AT, Carter RG, Welch KC, Stevens WW. Decreased nasal polyp eosinophils but increased mast cells in a patient with aspirin exacerbated respiratory disease treated with reslizumab. Ann Allergy Asthma Immunol. 2020 Oct;125(4):490-493.e2. doi: 10.1016/j.anai.2020.06.043. Epub 2020 Jul 4. PMID: 32629015; PMCID: PMC7529928.
23. Martínez-Moragón E, Climent M, Chiner E, Fernández-Aracil C, Sánchez-Toril F, Lluch-Tortajada I. Effectiveness and pharmacoeconomic analysis of the treatment of severe asthma with omalizumab in clinical practice. Farm Hosp. 2019 May 1;43(3):101-109. English. doi: 10.7399/fh.11167. PMID: 31072288.
24. Masieri S, Cavaliere C, Begvarfaj E, Rosati D, Minni A. Effects of omalizumab therapy on allergic rhinitis: a pilot study. Eur Rev Med Pharmacol Sci. 2016 Dec;20(24):5249-5255. PMID: 28051241.

25. Zhang Y, Xi L, Gao Y, Huang Y, Cao F, Xiong W, Wang C, Zhang L. Omalizumab is effective in the preseasonal treatment of seasonal allergic rhinitis. Clin Transl Allergy. 2022 Jan 4;12(1):e12094. doi: 10.1002/clt2.12094. PMID: 35024137; PMCID: PMC8727318.
26. Hutyrová B, Bystroň J; Czech Anti-IgE Registry collaborators. The effect of omalizumab treatment on severe allergic asthma and allergic comorbidities: real-life experience from the Czech Anti-IgE Registry. Postepy Dermatol Alergol. 2018 Oct;35(5):510-515. doi: 10.5114/ada.2018.77243. Epub 2018 Jul 19. PMID: 30429711; PMCID: PMC6232552.
27. Mosbech H, Canonica GW, Backer V, de Blay F, Klimek L, Broge L, Ljørring C. SQ house dust mite sublingually administered immunotherapy tablet (ALK) improves allergic rhinitis in patients with house dust mite allergic asthma and rhinitis symptoms. Ann Allergy Asthma Immunol. 2015 Feb;114(2):134-40. doi: 10.1016/j.anai.2014.11.015. PMID: 25624131.
28. Hoshino M, Akitsu K, Kubota K, Ohtawa J. Efficacy of a house dust mite sublingual immunotherapy tablet as add-on dupilumab in asthma with rhinitis. Allergol Int. 2022 Oct;71(4):490-497. doi: 10.1016/j.alit.2022.05.010. Epub 2022 Jun 17. PMID: 35718711.
29. Hébert J, Blaiss M, Waserman S, Kim H, Creticos P, Maloney J, Kaur A, Li Z, Nelson H, Nolte H. The efficacy and safety of the Timothy grass allergy sublingual immunotherapy tablet in Canadian adults and children. Allergy Asthma Clin Immunol. 2014 Oct 30;10(1):53. doi: 10.1186/1710-1492-10-53. PMID: 25685162; PMCID: PMC4326370.
30. Demoly P, Corren J, Creticos P, De Blay F, Gevaert P, Hellings P, Kowal K, Le Gall M, Nenasheva N, Passalacqua G, Pfaar O, Tortajada-Girbés M, Vidal C, Worm M, Casale TB. A 300 IR sublingual tablet is an effective, safe treatment for house dust mite-induced allergic rhinitis: An international, double-blind, placebo controlled, randomized phase III clinical trial. J Allergy Clin Immunol. 2021 Mar;147(3):1020-1030.e10. doi: 10.1016/j.jaci.2020.07.036. Epub 2020 Sep 2. PMID: 32890575.
31. Demoly P, Emminger W, Rehm D, Backer V, Tommerup L, Kleine-Tebbe J. Effective treatment of house dust mite-induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: Results from a randomized, double-blind, placebo controlled phase III trial. J Allergy Clin Immunol. 2016 Feb;137(2):444-451.e8. doi: 10.1016/j.jaci.2015.06.036. Epub 2015 Aug 17. PMID: 26292778.
32. Okamoto Y, Fujieda S, Okano M, Hida H, Kakudo S, Masuyama K. Efficacy of house dust mite sublingual tablet in the treatment of allergic rhinoconjunctivitis: A randomized trial in a pediatric population. Pediatr Allergy Immunol. 2019 Feb;30(1):66-73. doi: 10.1111/pai.12984. Epub 2018 Nov 25. PMID: 30281866; PMCID: PMC7379546.
33. Durham SR, Creticos PS, Nelson HS, Li Z, Kaur A, Meltzer EO, Nolte H. Treatment effect of sublingual immunotherapy tablets and pharmacotherapies for seasonal and perennial allergic rhinitis: Pooled analyses. J Allergy Clin Immunol. 2016 Oct;138(4):1081-1088.e4. doi: 10.1016/j.jaci.2016.04.061. Epub 2016 Jul 15. PMID: 27527264.
34. Valovirta E, Petersen TH, Piotrowska T, Laursen MK, Andersen JS, Sørensen HF, Klink R; GAP investigators. Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention

(GAP) trial in children with grass pollen allergy. J Allergy Clin Immunol. 2018 Feb;141(2):529-538.e13. doi: 10.1016/j.jaci.2017.06.014. Epub 2017 Jul 6. PMID: 28689794.

35. Brodowicz-Król M, Guz E, Hawryluk D, Kulbaka E, Panasiuk L, Lutomski P, Kaczor-Szkodny P, Choina P. Quality of life of patients undergoing specific allergen immunotherapy in allergic rhinitis. Ann Agric Environ Med. 2020 Dec 22;27(4):657-663. doi: 10.26444/aaem/127840. Epub 2020 Sep 29. PMID: 33356075.
36. Padró C, Gutiérrez D, Moreno F, Parra A, Rial MJ, Lleonart R, Torán-Barona C, Justicia JL, Roger A. Effectiveness and safety of a microcrystalline tyrosine adjuvanted Dermatophagoides pteronyssinus allergoid immunotherapy in adult patients with allergic asthma and rhinitis: A real-life prospective observational study. Immun Inflamm Dis. 2022 May;10(5):e585. doi: 10.1002/iid3.585. PMID: 35478444; PMCID: PMC9017636.
37. Mösges R, Koch AF, Raskopf E, Singh J, Shah-Hosseini K, Astvatsatourov A, Hauswald B, Yarin Y, Corazza F, Haazen L, Pirotton S, Allekotte S, Zadoyan G, Legon T, Durham SR, Shamji MH. Lolium perenne peptide immunotherapy is well tolerated and elicits a protective B-cell response in seasonal allergic rhinitis patients. Allergy. 2018 Jun;73(6):1254-1262. doi: 10.1111/all.13392. Epub 2018 Feb 13. PMID: 29322510; PMCID: PMC6032848.
38. Scadding GW, Eifan AO, Lao-Araya M, Penagos M, Poon SY, Steveling E, Yan R, Switzer A, Phippard D, Togias A, Shamji MH, Durham SR. Effect of grass pollen immunotherapy on clinical and local immune response to nasal allergen challenge. Allergy. 2015 Jun;70(6):689-96. doi: 10.1111/all.12608. Epub 2015 Apr 6. Erratum in: Allergy. 2015 Aug;70(8):1033. doi: 10.1111/all.12659. PMID: 25773990; PMCID: PMC4826905.
39. Roger A, Malet A, Moreno V, Parra A, Gutiérrez D, Lleonart R, Moreno F, Valero A, Navarro B, Hinojosa B, Justicia JL. Real-life effect of a microcrystalline tyrosine adjuvanted mite immunotherapy in patients with allergic rhinitis. Immunotherapy. 2020 Jan;12(1):53-62. doi: 10.2217/imt-2019-0205. Epub 2020 Jan 8. PMID: 31910695.
40. Baiardini I, Puggioni F, Menoni S, Boot JD, Diamant Z, Braido F, Canonica GW. Patient knowledge, perceptions, expectations and satisfaction on allergen specific immunotherapy: a survey. Respir Med. 2013 Mar;107(3):361-7. doi: 10.1016/j.rmed.2012.11.004. Epub 2012 Dec 4. PMID: 23218454.
41. Qiu Q, Xu M, Lu C, Chen J, Chen S, Kong W, Han H. Safety and efficacy of rush allergen-specific immunotherapy in Chinese allergic rhinitis patients. Int J Immunopathol Pharmacol. 2016 Dec;29(4):720-725. doi: 10.1177/0394632016659301. Epub 2016 Aug 10. PMID: 27510816; PMCID: PMC5806822.
42. Yang L, Yang Y, Xu Q, Zhang W, Jiang Q, Li W, Wang Y, Ma D, Lin X, Sun B, Zhu R. Specific IgE and IgG4 Profiles of House Dust Mite Components in Allergen-Specific Immunotherapy. Front Immunol. 2022 Feb 7;12:786738. doi: 10.3389/fimmu.2021.786738. PMID: 35197963; PMCID: PMC8858833.
43. Bozek A, Kolodziejczyk K, Jarzab J. Safety and efficacy of tree pollen specific immunotherapy on the ultrarush administration schedule method using purethal trees. Biomed Res Int. 2014;2014:707634. doi: 10.1155/2014/707634. Epub 2014 Mar 24. PMID: 24783221; PMCID: PMC3982251.

44. Berge M, Bertilsson L, Hultgren O, Hugosson S, Saber A. Pre-treatment allergen-specific IgE analysis and outcomes of allergen immunotherapy. Eur Ann Allergy Clin Immunol. 2022 Sep;54(5):218-228. doi: 10.23822/EurAnnACI.1764 1489.199. Epub 2021 May 3. PMID: 33939346.
45. Lourenço EA, Caldeira EJ, Carvalho CA, Cunha MR, Carvalho MV, Passos SD. Subcutaneous Immunotherapy Improves the Symptomatology of Allergic Rhinitis. Int Arch Otorhinolaryngol. 2016 Jan;20(1):6-12. doi: 10.1055/s-0035 1564437. Epub 2015 Oct 7. PMID: 26722338; PMCID: PMC4688001.
46. Saenza De San Pedro B, Mur MP, Valverde L, Gonzalo Garijo MA, Hernandez M, Madariaga B, Asturias JA, Begona L, Martinez A, Gomez Fernandez M. Clinical 82 assessment of tolerability, immunological and cutaneous reactivity effects of an abbreviated schedule with Olea europaeanative extract of subcutaneous immunotherapy. Eur Ann Allergy Clin Immunol. 2020 Sep;52(5):210-219. doi: 10.23822/EurAnnACI.1764-1489.124. Epub 2020 Sep 7. PMID: 31789492.
47. Cardona-Villa R, Uribe-Garcia S, Calvo-Betancur VD, Cantillo JF, Fernández Caldas E. Efficacy and safety of subcutaneous immunotherapy with a mixture of glutaraldehyde-modified extracts of Dermatophagoides pteronyssinus, Dermatophagoides farinae, and Blomia tropicalis. World Allergy Organ J. 2022 Sep 8;15(9):100692. doi: 10.1016/j.waojou.2022.100692. PMID: 36119655; PMCID: PMC9467880.
48. Corren J, Saini SS, Gagnon R, Moss MH, Sussman G, Jacobs J, Laws E, Chung ES, Constant T, Sun Y, Maloney J, Hamilton JD, Ruddy M, Wang CQ, O'Brien MP. Short-Term Subcutaneous Allergy Immunotherapy and Dupilumab are Well Tolerated in Allergic Rhinitis: A Randomized Trial. J Asthma Allergy. 2021 Aug 68 16;14:1045-1063. doi: 10.2147/JAA.S318892. PMID: 34429614; PMCID: PMC8379710.
49. Pothirat C, Chaiwong W. A Real-World Effectiveness of Subcutaneous Immunotherapy on the Cost of Medication, Allergic Rhinitis, and Asthma Exacerbations, as well as Upper Respiratory Tract Infection in Subjects with Allergic Rhinitis with or without Asthma: A Retrospective Pilot Study. Medicina (Kaunas). 2021 Nov 11;57(11):1229. doi: 10.3390/medicina57111229. PMID: 34833447; PMCID: PMC8619032.
50. Caruso C, Colantuono S, Tolusso B, Di Mario C, Fancello G, La Sorda M, Celi G, Caringi M, Volterrani A, Descalzi D, Gremese E, Sanguinetti M, Gasbarrini A, Canonica GW. Effects of house dust mite subcutaneous immunotherapy in real life. Immunological and clinical biomarkers and economic impact analysis. World Allergy Organ J. 2023 Jun 15;16(6):100789. doi: 10.1016/j.waojou.2023.100789. PMID: 37484874; PMCID: PMC10362513.
51. Kim CK, Callaway Z, Park JS, Kwon E. Efficacy of subcutaneous immunotherapy for patients with asthma and allergic rhinitis in Korea: effect on eosinophilic inflammation. Asia Pac Allergy. 2021 Oct 25;11(4):e43. doi: 10.5415/apallergy.2021.11.e43. PMID: 34786373; PMCID: PMC8563102.
52. Su Q, Ren N, Feng M, Zeng X, Dong Y, Xian M, Shi X, Luo T, Liu G, Li J. Specific immunoglobulin G4 correlates with Th2 cytokine reduction in patients 84 with allergic asthma treated by Dermatophagoides pteronyssinus subcutaneous immunotherapy. World Allergy Organ J. 2023 Jan 26;16(1):100715. doi: 10.1016/j.waojou.2022.100715. PMID: 36820309; PMCID: PMC9937843.

53. Lee JH, Kim SC, Choi H, Jung CG, Ban GY, Shin YS, Nahm DH, Park HS, Ye YM. Subcutaneous Immunotherapy for Allergic Asthma in a Single Center of Korea: Efficacy, Safety, and Clinical Response Predictors. J Korean Med Sci. 2017 Jul;32(7):1124-1130. doi: 10.3346/jkms.2017.32.7.1124. PMID: 28581269; PMCID: PMC5461316.
54. Vieira-Hernández A, Capriles-Hulett A, Sánchez-Borges M, Fabiano F, Albarrán-Barrios C. Inmunoterapia intradérmica con alérgenos de ácaros a bajas dosis en pacientes con rinitis alérgica: un estudio conceptual [Intradermal immunotherapy with low-dose house dust mite allergens in patients with allergic rhinitis: A proof-of-concept study]. Rev Alerg Mex. 2018 Jan-Mar;65(1):41-51. Spanish. doi: 10.29262/ram.v65i1.322. PMID: 29723940.
55. [55] Ahlbeck L, Ahlberg E, Björkander J, Aldén C, Papapavlou G, Palmberg L, Nyström U, Retsas P, Nordenfelt P, Togö T, Johansen P, Rolander B, Duchén K, Jenmalm MC. Intralymphatic immunotherapy with one or two allergens renders similar clinical response in patients with allergic rhinitis due to birch and grass pollen. Clin Exp Allergy. 2022 Jun;52(6):747-759. doi: 10.1111/cea.14138. Epub 2022 Apr 1. PMID: 35332591; PMCID: PMC9325375.
56. Ahlbeck L, Ahlberg E, Stuivers L, Björkander J, Nyström U, Retsas P, Govindaraj D, Jenmalm MC, Duchén K. Intralymphatic immunotherapy with birch and grass pollen extracts. A randomized double-blind placebo-controlled clinical trial. Clin Exp Allergy. 2023 Aug;53(8):809-820. doi: 10.1111/cea.14307. Epub 2023 Apr 4. PMID: 37013723; PMCID: PMC10947267.
57. Hjalmarsson E, Hellkvist L, Karlsson A, Winquist O, Kumlien Georén S, Westin U, Cardell LO. A 5-Year Open-Label Follow-up of a Randomized Double-Blind Placebo-Controlled Trial of Intralymphatic Immunotherapy for Birch and Grass Allergy Reveals Long-term Beneficial Effects. J Investig Allergol Clin Immunol. 2023 Oct;33(5):362-372. doi: 10.18176/jiaci.0832. PMID: 37843385.
58. Iinuma T, Kiuchi M, Hirahara K, Kurita J, Kokubo K, Yagyu H, Yoneda R, Arai T, Sonobe Y, Fukuyo M, Kaneda A, Yonekura S, Nakayama T, Okamoto Y, Hanazawa T. Single-cell immunoprofiling after immunotherapy for allergic rhinitis reveals functional suppression of pathogenic TH2 cells and clonal conversion. J Allergy Clin Immunol. 2022 Oct;150(4):850-860.e5. doi: 10.1016/j.jaci.2022.06.024. Epub 2022 Jul 19. PMID: 35863510.
59. De Castro G, Zicari AM, Indinnimeo L, Tancredi G, di Coste A, Occasi F, Castagna G, Giancane G, Duse M. Efficacy of sublingual specific immunotherapy on allergic asthma and rhinitis in children's real life. Eur Rev Med Pharmacol Sci. 2013 Aug;17(16):2225-31. PMID: 23893190.
60. Didier A, Campo P, Moreno F, Durand-Perdriel F, Marin A, Chartier A. Dose Dependent Immunological Responses after a 6-Month Course of Sublingual House Dust Mite Immunotherapy in Patients with Allergic Rhinitis. Int Arch Allergy Immunol. 2015;168(3):182-92. doi: 10.1159/000442467. Epub 2016 Jan 21. PMID: 26789997.
61. Novakova SM, Staevska MT, Novakova PI, Yoncheva MD, Bratoycheva MS, Musurlieva NM, Tzekov VD, Nicolov DG. Quality of life improvement after a three year course of sublingual immunotherapy in patients with house dust mite and grass pollen induced allergic rhinitis: results from real-life. Health Qual Life 78 Outcomes. 2017 Sep 29;15(1):189. doi: 10.1186/s12955-017-0764-z. PMID: 28962623; PMCID: PMC5622572.

62. Han M, Chen Y, Wang M. Sublingual immunotherapy for treating adult patients with allergic rhinitis induced by house dust mite among Chinese Han population: A retrospective study. Medicine (Baltimore). 2018 Jul;97(30):e11705. doi: 10.1097/MD.0000000000011705. PMID: 30045332; PMCID: PMC6078716.
63. Lim JH, Kim JY, Han DH, Lee CH, Hong SN, Wee JH, Park SK, Rhee CS. Sublingual immunotherapy (SLIT) for house dust mites does not prevent new allergen sensitization and bronchial hyper-responsiveness in allergic rhinitis children. PLoS One. 2017 Aug 14;12(8):e0182295. doi: 10.1371/journal.pone.0182295. PMID: 28806766; PMCID: PMC5555666.
64. Bovermann X, Ricklefs I, Vogelberg C, Klimek L, Kopp MV. Accelerated Dose Escalation with 3 Injections of an Aluminum Hydroxide-Adsorbed Allergoid Preparation of 6 Grasses Is Safe for Children and Adolescents with Moderate to Severe Allergic Rhinitis. Int Arch Allergy Immunol. 2021;182(6):524-534. doi: 10.1159/000512561. Epub 2021 Jan 27. PMID: 33503610.
65. Soyyiğit S, Aydın Ö, Seçil D, Doğan C, Gökmen D, Sin BA, Mısırlıgil Z, Mungan VD. Pre-seasonal immunotherapy is effective in both monosensitized and polysensitized patients with allergic rhinitis. Eur Ann Allergy Clin Immunol. 2023 May;55(3):122-130. doi: 10.23822/EurAnnACI.1764-1489.252. Epub 2022 Apr 22. PMID: 35448936.

Figures

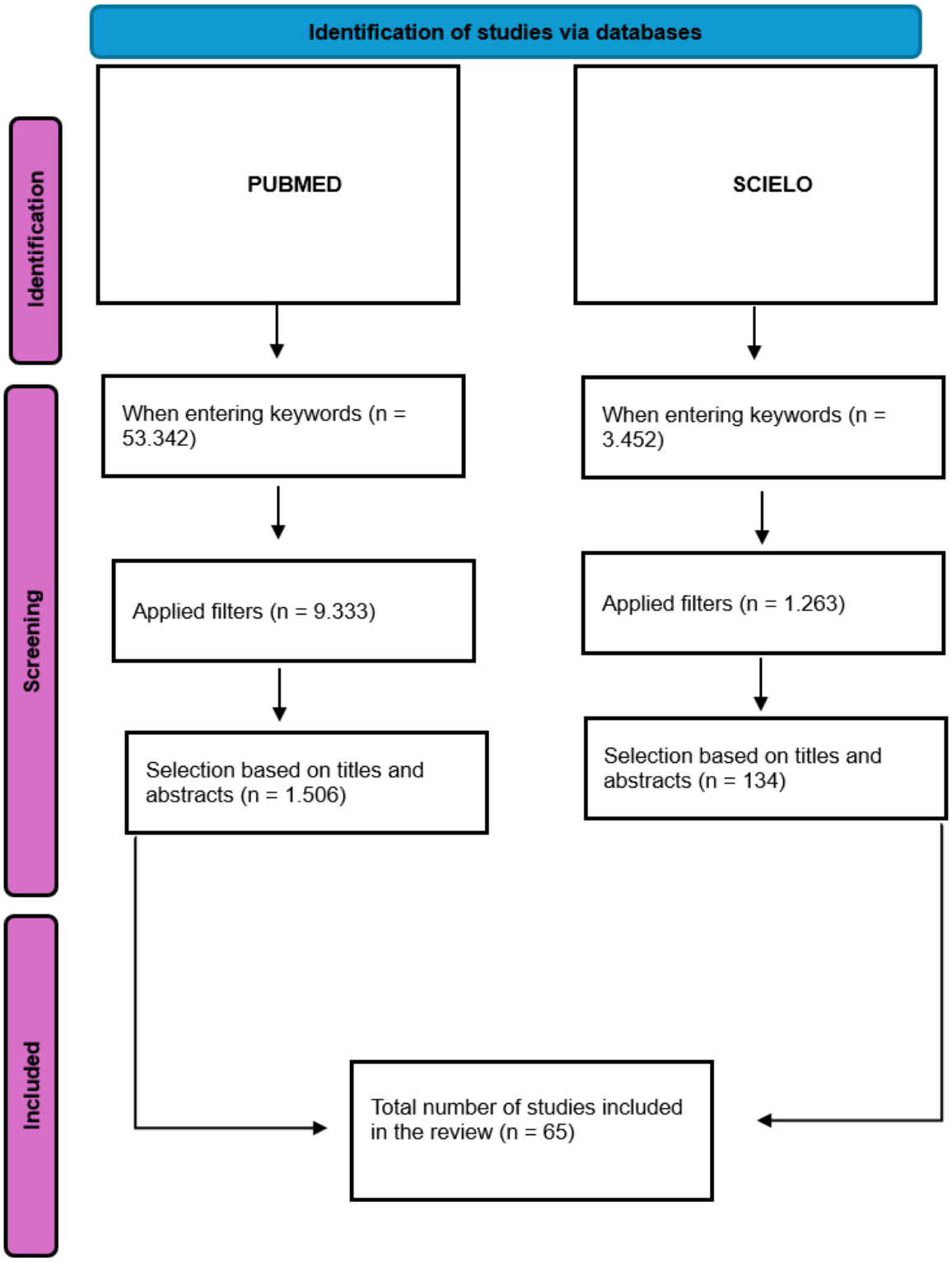

Figure 1

Flowchart of the literature search and study-selection process.

Source: Prepared by the authors.