Biologic Therapies for Immunoglobulin E–mediated Food Allergy and Eosinophilic Esophagitis

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KEYWORDS

• Food allergy • Eosinophilic esophagitis • Anti-IgE • Anti–IL-5 • Anti–IL-13 • QAX576 • OC000459

KEY POINTS

- Immunoglobulin (Ig) E–mediated food allergy and eosinophilic esophagitis (EoE) are chronic, allergen-mediated disorders.
- Investigation of biologic therapies in IgE-mediated food allergy and EoE have provided insights into the pathophysiology and treatment of these disorders.
- In IgE-mediated food allergy, anti-IgE therapy seems to increase tolerability of food allergens and safety of oral desensitization protocols, although further larger studies are necessary to further elucidate the most safe and effective use of anti-IgE.
- In EoE, the use of biologics targeting interleukin (IL)-5, IL-13, IgE, and the CRTH2 receptors, have had mixed results. Decreases in esophageal eosinophilia were not necessarily accompanied by symptomatic remission.
- Identification of EoE phenotypes that are responsive to biologics and investigation of biologics in combination with other therapies may help elucidate a role for biologic therapy in EoE.

INTRODUCTION

Food allergy is defined as an aberrant immune response to food proteins leading to mucocutaneous, gastrointestinal, and/or respiratory symptoms. Food allergy can encompass purely IgE-mediated food allergy as well as mixed IgE-mediated and non–IgE-mediated disease, such as eosinophilic esophagitis (EoE).[1] The development

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and investigation of biologics for the treatment of IgE-mediated food allergy and EoE have provided further insight into the pathophysiology and management of these disorders. This article provides an overview of biologic therapies that are being investigated or have potential as treatments for IgE-mediated food allergy and EoE.

IMMUNOGLOBULIN E–MEDIATED FOOD ALLERGY

The prevalence of food allergy has been estimated at 8% in children and 5% in adults.[2] Although the incidence of food allergy continues to increase,[3] allergen avoidance and treatment of accidental ingestion with epinephrine remain the only US Food and Drug Administration (FDA)–approved treatments.[4] Allergen avoidance and fear of accidental ingestion are associated with stress and anxiety that significantly impair quality of life for affected children and their caregivers.[5]

Food allergen immunotherapy via oral, sublingual, and epicutaneous routes is being actively investigated as a treatment of IgE-mediated food allergy. Gradually increasing exposure to food allergens can lead to desensitization and induce immune tolerance to food allergens. The safety and efficacy of immunotherapy for food allergy remain unclear, because adverse reactions can occur and tolerance has been shown to wane after active immunotherapy is discontinued.[6,7]

Anti–Immunoglobulin E for Immunoglobulin E–Mediated Food Allergy

IgE-mediated food allergy reactions occur when mast cells and basophils are activated after allergen exposure through cross-linking of preformed allergen-specific IgE on the cell surface.[8] Anti-IgE is under investigation both as a stand-alone therapy and an adjunctive treatment that could potentially improve the safety and efficacy of allergen immunotherapy (**Table 1**).

Omalizumab

Omalizumab (Xolair; Genentech, South San Francisco, CA) is a humanized IgG_1 monoclonal antibody (mAb) that binds the Fc region of IgE and blocks the binding of IgE to its high-affinity FcεRI on mast cells, basophils, and dendritic cells, thereby interrupting the allergic cascade.[18] It is administered subcutaneously and is FDA approved for moderate to severe persistent allergic asthma inadequately controlled with inhaled corticosteroids in patients 12 years of age or older.[19] Omalizumab is also FDA approved for chronic idiopathic urticaria inadequately controlled with H1 antihistamines in patients 12 years of age or older.[20]

For allergic asthma, dosing is calculated based on pretreatment serum IgE levels and body weight, with dosages ranging between 150 to 375 mg administered subcutaneously every 2 to 4 weeks.[19] For chronic idiopathic urticaria, the dosage is between 150 to 300 mg administered subcutaneously every 4 weeks, independent of serum IgE level or body weight.[20]

Omalizumab can exert several biological effects in allergic disease. It can significantly reduce FcεRI expression on basophils and plasmacytoid dendritic cells,[21–24] decrease serum IgE levels,[25,26] and decrease allergen-specific basophil reactivity[27] and histamine release.[28,29] It has been investigated both as a stand-alone and adjunctive therapy to allergen immunotherapy in allergic rhinitis and as a therapy for atopic dermatitis, with mixed results.[20]

Talizumab

Talizumab (TNX-901; Tanox, Houston, TX) is a humanized IgG_1 mAb administered subcutaneously. Like omalizumab, talizumab binds the Fc region of IgE, blocking IgE binding to FcεRI.[18]