Three hundred million people suffer from asthma. Despite recent guidelines and multiple therapies, 40% of adult asthmatics and 5% of patients with uncontrolled asthma have persisting symptoms. They may need a new asthma drug.

Knowing the central role of Immunoglobulin E (IgE) in inflammation of allergic asthma, a monoclonal antibody against IgE – anti-IgE – was developed, designed to inhibit the allergic inflammatory response, characterising asthma.

Anti-IgE binds free IgE at the Cb3 domain of its Fc fragment. Treatment with anti-IgE results in: decrease of free IgE and of expression of FcdRI receptors on basophils, mast cells and other inflammatory cells; decrease in airway and tissue eosinophilia in asthmatic patients; decrease of T-B-lymphocyte and IL-4+ cells and decreased peripheral blood eosinophilia.

Patients with allergic asthma, receiving anti-IgE, had fewer asthma exacerbations and decreased the daily steroid-dose by 100 μg according to a recent meta-analysis. However, surprisingly, their symptoms, lung function or bronchial hyperreactivity did not improve.

The reduced blood and airways eosinophilia, induced by anti-IgE, might be partly explained by inhibition of the allergen–IgE–mast cell response. Thus, anti-IgE reduces IgE, empties its receptors, decreases their number on basophils, mast and dendritic cells, preventing their activation, cytokine release and chemotaxis of eosinophils, inhibiting the acute allergic reaction and preventing influx of inflammatory cells, tissue remodelling, and functional changes of airways.

Anti-IgE inactivates epithelial and smooth muscle cells bearing the low-affinity IgE receptor (CD23), thus decreasing eosinophilia in the lower and upper airways and the skin. Pre-treatment of allergen-sensitised mice with anti-IgE, inhibits the production of TH2 cytokines and recruitment of eosinophils to the lung, possibly through inhibition of IgE-CD23. The anti-IgE effects may appear early or later (days-weeks) interpreted by anti-IgE’s disrupting weak IgE-CD23 or strong IgE-FcdRI interactions, respectively.

Anti-IgE also inhibits the number of FcdRI on dendritic cells. This may decrease the presentation of antigen to T cells, prevent active inflammatory cells from secreting mediators and cytokines, (IL-5), causing airway eosinopenia. Since allergen presentation is critical for starting the allergic cascade, this anti-IgE effect possibly drives the treatment of allergic diseases to a significant new direction.

Anti-IgE reduces the underlying airway inflammation and prevents its worsening after allergen exposure, frequently preceding an asthma exacerbation. Thus, the activity of anti-IgE against IgE, inflammatory and dendritic cells inhibits IgE-mediated hypersensitivity but also causes immunomodulation on allergen-specific T cells. This function may prevent sensitisation and the accompanied inflammation, particularly in moderate to severe allergic asthmatics. These multiple anti-inflammatory effects of anti-IgE may offer a new treatment to other IgE-mediated disorders.

The effectiveness of anti-IgE in decreasing asthma exacerbations, without affecting bronchial hyperreactivity or FEV1, suggests that the IgE-associated effect may relate less to airway smooth muscle hyperreactivity and more to other causes of exacerbation, such as mucus hypersecretion and/or bronchovascular leaking.

In conclusion, anti-IgE is a new promising treatment for selective patients. The anti-IgE reduction of exacerbation, in asthmatic patients, through decreasing eosinophilia, without improvement of FEV1 or airway hyperresponsiveness, demonstrates that many factors linking inflammation, hyperresponsiveness, remodelling, and airway function, in asthma, are still unknown.
REFERENCES


