Inhaled corticosteroids (ICS) are the mainstay of anti-inflammatory treatment for both asthma and chronic obstructive pulmonary disease (COPD). Many asthma patients have poorly controlled disease despite high ICS doses administered in combination with a long acting beta agonist (LABA). Similarly, ICS/LABA combinations often fail to adequately prevent exacerbations and improve symptoms, even when given with a long acting muscarinic antagonist (“triple therapy”). There is an unmet medical need for novel anti-inflammatory therapies for asthma patients who are poorly controlled on ICS/LABA treatment, and for COPD patients who suffer with exacerbations despite treatment with triple therapy.

Asthma and COPD consist of subgroups of patients that have different clinical characteristics; these are called clinical phenotypes. Endotypes are subgroups defined by distinct biological mechanisms that contribute to disease pathophysiology. Endotypes give rise to clinical features, and individual patients often express more than one endotype. Existing treatments (ICS and bronchodilators) are targeted towards clinical features e.g. symptoms and exacerbations. However, novel anti-inflammatory approaches that selectively target biological mechanisms may be more effectively targeted towards patients who express the target endotype. The development of biomarkers that identify endotypes is important for the success of this approach. The benefit of this approach is to optimise the therapeutic index by identifying patients most likely to gain clinical benefit.

It has been estimated that approximately half of the patients with moderate to severe asthma have excessive type 2 (T2) immunity. Novel monoclonal antibodies targeting different T2 processes have shown clinical efficacy in asthma. For example, interleukin-5 (IL-5) is a cytokine that promotes eosinophil activation and recruitment from the bone marrow; Humanized monoclonal antibodies directed against IL-5 or the IL-5 receptor improve lung function and reduce exacerbation rates in moderate to severe asthma patients with eosinophilic inflammation. Another example of targeting T2 inflammation is the development of humanized monoclonal antibodies against the cytokine IL-13, which has multiple roles in airway inflammation and remodeling [1]. These treatments target the IL-13 receptor, or both IL-13 and IL-4 receptors; these monoclonal antibodies reduce exacerbation rates and improve lung function in moderate to severe asthma. Periostin, which is secreted by bronchial epithelial cells in response to IL-13 stimulation, has been used as a serum biomarker to identify patients with a greater clinical response. The optimal use of blood eosinophils, serum periostin and exhaled nitric oxide as biomarkers to select individuals most likely to respond to these different biological interventions has yet to be defined. While there are a range of promising novel biological therapies targeting T2 inflammation in asthma, the development of novel treatments against non-T2 inflammation is much less advanced.

Targeting eosinophils in COPD is an interesting avenue, with a phase II study showing some evidence of efficacy. Eosinophils appear to play a role in airway inflammation in a subset of COPD patients, and larger trials are ongoing to further evaluate the role of anti-IL5 based treatments in COPD.

In summary, novel monoclonal antibody approaches have demonstrated clinical efficacy in moderate to severe asthma. There are challenges now to further optimise the use of biomarkers to select the appropriate patients to receive these treatments.
References


