Lung alert

Mepolizumab in corticosteroid-resistant eosinophilic asthma

Eosinophils have long been regarded as a key inflammatory cell mediator in the pathogenesis of asthma, although their exact role is unclear. Downregulation of eosinophil activity via targeted interleukin 5 (IL5) inhibition (a pro-eosinophilic cytokine) in the study of heterogeneous populations of subjects with asthma has yielded disappointing results.

Two recent well-designed randomised controlled trials have investigated the safety and efficacy of selected IL5 inhibition with mepolizumab (monoclonal antibody against IL5) in a subset of patients with corticosteroid-resistant eosinophilic asthma. These patients represent a minority of patients with asthma.

In the first study, patients were stratified into two groups according to their daily dose of prednisolone (<10 mg or >10 mg), then randomised to receive either mepolizumab (750 mg intravenously, n = 9) or placebo (150 ml 0.9% saline, n = 11) as five monthly infusions. After a 6-week run-in period, prednisolone dose reduction was attempted according to a predefined protocol.

The second study had a run-in period of 2 weeks prednisolone (1 mg/kg to a maximum of 40 mg), following which 61 patients were randomised to receive 12 infusions of either mepolizumab (750 mg intravenously, n = 29) or placebo (150 ml 0.9% saline, n = 32) at monthly intervals.

Both studies demonstrated a statistically significant reduction in asthma exacerbation frequency accompanied by a significant reduction in blood and sputum eosinophils. Despite this, neither study identified any clinically meaningful improvement in symptoms, forced expiratory volume in 1 s or asthma control. No serious adverse events were recorded in either study population.

Improvement in asthma lung function and symptoms was demonstrated with corticosteroid therapy alone, reflecting the heterogeneity of this disease and implying a complex interaction of a host of inflammatory cell types, of which eosinophils play just one part. In summary, these studies do suggest that, in a subgroup of patients, eosinophils are an important contributor to the pathophysiology of asthmatic exacerbations. These patients may benefit from targeted IL5 therapy with mepolizumab.


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