

JOURNAL CLUB

Dupilumab in persistent asthma with elevated eosinophil levels

Monoclonal antibodies are an effective treatment for a number of inflammatory autoimmune conditions, particularly those refractory to first-line medications. In asthma, airway inflammation may be associated with Th2 cell overactivity and raised eosinophils in up to 50% of cases. Th2 activation leads to the release of interleukin (IL)-13 and IL-4, which mediate their effects via receptors containing the IL-4 α subunit. Dupilumab is an IL-4 α subunit inhibitor aiming to block both signalling pathways and reduce airway inflammation.

The authors conducted a randomised, double-blind, placebo-controlled study to evaluate the effectiveness and safety of dupilumab in the treatment of persistent moderate-to-severe asthma. They recruited 104 patients, aged 18–65, who had an elevated blood or sputum eosinophil count and symptoms that remained poorly controlled despite medium-dose to high-dose inhaled corticosteroid (ICS) and long-acting bronchodilators (LABAs). Patients received once-weekly subcutaneous injections of dupilumab or placebo for 12 weeks or until they suffered an asthma exacerbation. LABAs were discontinued at week 4, and ICSs tapered from week 6 to stop by week 9.

The primary outcome was an asthma exacerbation requiring systemic steroids or hospital attendance. This was seen in 6% of those receiving dupilumab and 44% of those receiving placebo. In terms of secondary outcomes, dupilumab patients showed significant improvements in FEV₁, morning peak respiratory flow rate, asthma symptoms, nocturnal awakening, salbutamol use and Th2-associated inflammatory markers.

These promising results warrant further investigation over a longer time frame. Adverse effects, notably injection-site reactions, nasopharyngitis, nausea and headache, were reported more frequently with dupilumab; hence, further studies are required to determine its long-term safety and side-effect profile, something that may ultimately affect patient compliance.

► Wenzel S, Ford L, Pearlman D, *et al.* Dupilumab in persistent asthma with elevated eosinophil levels. *N Engl J Med* 2013;368:2455–66.

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