Medical Xpress

Benralizumab injections reduce exacerbations in severe, uncontrolled asthma, according to two trials

September 5 2016

A year's course of benralizumab injections has led to a significant decrease in the frequency of asthma exacerbations - cutting the rate of exacerbations by a third to a half compared with placebo among people with the most severe form of asthma, according to two phase 3, double-blind, randomised controlled trials including more than 2500 patients in total.

The two trials, published in *The Lancet* and presented at the European Respiratory Society meeting in London, looked at the safety and efficacy of benralizumab as an add-on therapy for patients with severe, uncontrolled asthma - a group of patients who have few treatment options available and high rates of hospitalisation.

Asthma affects an estimated 315 million people worldwide, approximately 10% of whom have severe or uncontrolled asthma. Patients with severe asthma require treatment with high-dose inhaled corticosteroids (ISC) and long-acting beta agonists (LABA) to control the illness - both are delivered in the form of inhalers. However, for some patients, current treatments fail to control their asthma and they remain at high risk of exacerbations and hospitalisation.

Eosinophils are a type of white blood cell and part of the immune system controlling the mechanism associated with allergy and asthma. Many patients with severe, uncontrolled asthma have high levels of eosinophils

in the blood and airways (known as eosinophilia) which is associated with frequent asthma exacerbations, high symptom burden and impaired lung function.

Cytokine interleukin-5 (IL-5) is the main driver of eosinophil proliferation, maturation, activation and survival. Two currently available drugs, mepolizumab and reslizumab, target the IL-5 molecule itself to stop the process of eosinophil maturation. Benralizumab, on the other hand, uses a different pathway by targeting the IL-5 receptor, causing eosinophil apoptosis (cell death).

In the CALIMA trial, 1306 patients aged 12-75 with severe asthma were randomly allocated into three groups: benralizumab 30mg every 4 weeks; benralizumab 30mg every 8 weeks (first 3 doses at 4 weeks apart); or placebo. Treatment continued for 56 weeks. All patients were already being treated with ISC and LABA and had experienced at least two exacerbations in the previous year.

The aim of the trial was to measure the effect of the drug on the annual rate of exacerbations in a sub-group of 728 patients with high eosinophils counts (over 300 cells/microL) - the most severe form of asthma. Benralizumab resulted in a 28-36% reduction in exacerbation rates compared to placebo (reduction from 2.8 to 0.60 exacerbations per year for treatment every 4 weeks; 2.7 to 0.66 for treatment every 8 weeks; 2.8 to 0.93 for placebo) (table 1 & 2). Benralizumab also resulted in improved lung function (as measured via spirometry) and total asthma score (treatment every 8 weeks only).

The most common adverse events were nasopharyngitis (169 [20%] of 866 benralizumab-treated patients vs 90 [21%] of 440 placebo-treated patients) and worsening asthma (108 [12%] vs 68 [15%]) (table 4). Four patients experienced serious adverse events which were considered related to treatment: one case of uricaria (hives) and two cases of asthma

and herpes zoster in the benralizumab-treated group, and one case of non-cardiac chest pain the placebo-treated group. Seven (