Researchers identify new choice of therapy for rare autoimmune disease EGPA

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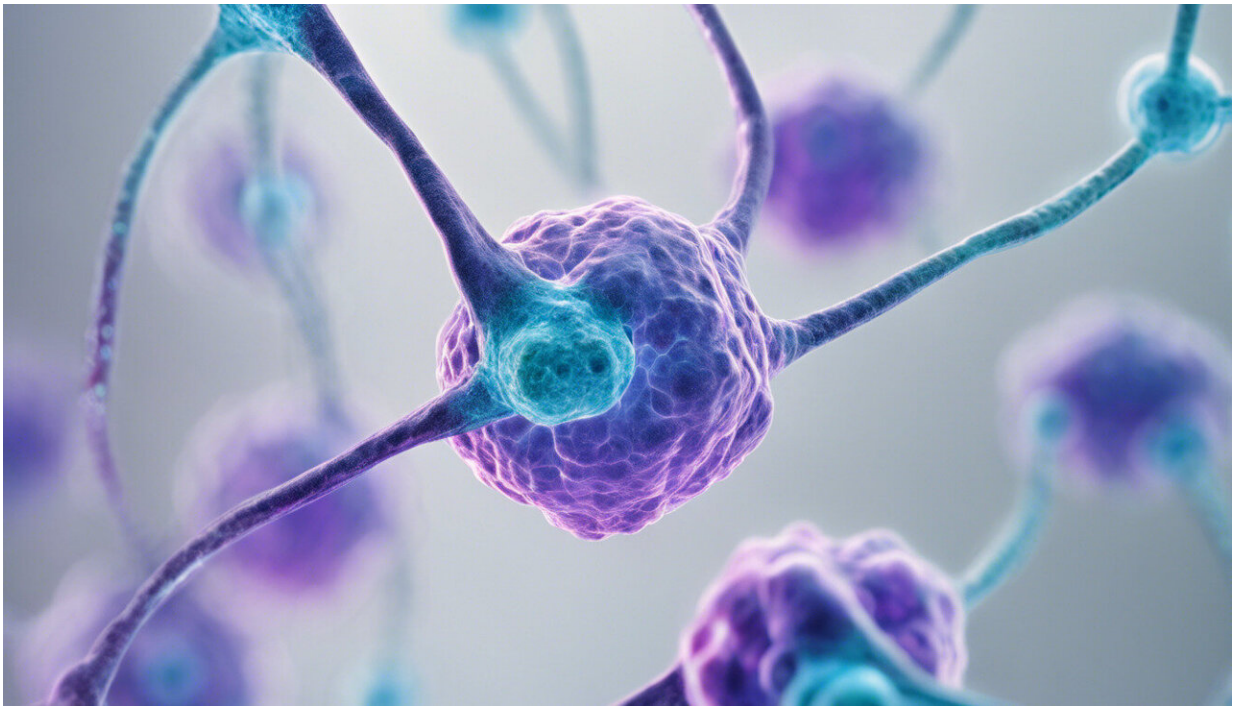

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An international team has identified a new therapeutic for patients with a rare autoimmune disease called eosinophilic granulomatosis with polyangiitis (EGPA). A biologic drug called benralizumab has been shown to be non-inferior to mepolizumab in the treatment of EGPA.

In a clinical trial involving 140 patients with the rare disease, researchers directly compared two biologic drugs, mepolizumab and benralizumab. Patients received monthly subcutaneous injections of either 300 mg of mepolizumab or 30 mg of benralizumab for one year. The findings of the trial were published on Feb. 23, 2024, in the *New England Journal of Medicine*.

"Our findings show that benralizumab was just as effective as mepolizumab at reducing exacerbations and providing disease remission during the 52 weeks of the study," says Parameswaran Nair, a professor with McMaster's Department of Medicine and a respirologist at St. Joe's Firestone Institute for Respiratory Health.

Nair was one of the study's principal investigators who led the Canadian team. He worked closely with Nader Khalidi, a professor with McMaster's Department of Medicine and a rheumatologist with St. Joe's, to design the study and recruit patients.

"The single 30 mg subcutaneous dosing of benralizumab offers an advantage to patients over the three 100 mg subcutaneous dosing of mepolizumab," says Nair.

EGPA, also known as Churg-Strauss Syndrome, is a rare autoimmune disease caused by inflammation of small and medium sized blood vessels and is associated with very high blood and tissue eosinophil counts. This can lead to damage of the lungs, skin, heart, gastrointestinal tract, and nerves. Most patients with EGPA experience breathing and lung issues.

The researchers noted that approximately 16 percent more patients in the benralizumab group were able to abstain from using oral corticosteroids compared to the mepolizumab group. Typically, patients with EGPA use oral corticosteroids like prednisone for symptom control despite the adverse effects.

"Without biologics, we're relying predominantly on oral corticosteroids to control EGPA symptoms. Prolonged treatment with prednisone reduces the risk of a relapse of EGPA symptoms, but it comes with progressive toxic effects," says Khalidi. "In our study, treatment with benralizumab allowed more patients to discontinue prednisone over a 52-week period compared to mepolizumab."

Mepolizumab and benralizumab are biologic drugs. Biologics are a class of drugs that come from living organisms or from their cells, often made using biotechnology.

The two biologics used in this study work by targeting either the signals or the receptors of eosinophils, a type of immune cell that is found in high concentrations in the blood and tissue of EGPA patients. By blocking the signals or receptors that draw eosinophils into various tissues, such as the lungs, mepolizumab and benralizumab effectively decrease eosinophils, reducing symptoms.

"Benralizumab was associated with greater blood eosinophil depletion than mepolizumab from week one onwards," says Nair. "Both drugs were well tolerated without any new adverse events."

The study builds on a long history of research on eosinophilic conditions from the Firestone Institute for Respiratory Health at St. Joe's. Pioneering work into the study of severe eosinophilic asthma by Freddy Hargreave led to a method for enumerating eosinophils in sputum samples for accurate asthma diagnoses.

For patients with severe prednisone-dependent asthma, Hargreave, Nair, and their colleagues were the first to demonstrate the efficacy of mepolizumab in 2009. By 2017, Nair had further demonstrated the efficacy of benralizumab for the same condition. Both landmark studies were published in the *New England Journal of Medicine*.

"It is very gratifying that our research program at the Firestone Institute at St. Joe's has led to the development of these new treatment options for patients with severe eosinophilic diseases," Nair says.

More information: Michael E. Wechsler et al, Benralizumab versus Mepolizumab for Eosinophilic Granulomatosis with Polyangiitis, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2311155

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