International study supports dupilumab for treatment of moderate-to-severe asthma in children

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A new medication has been added to the treatment options for children with moderate-to-severe asthma. In a late-stage clinical trial, the biologic

agent dupilumab reduced the rate of severe asthma attacks and improved lung function and asthma control for children ages 6 to 11.

The findings of the international multicenter Liberty Asthma VOYAGE trial, reported Dec. 9 in the *New England Journal of Medicine*, supported approval of dupilumab for the treatment of moderate-to-severe asthma in this age group by the Food and Drug Administration in October.

"This is a really important advance for children with moderate-to-severe asthma and their families," said Leonard Bacharier, MD, an asthma specialist at Monroe Carell Jr. Children's Hospital at Vanderbilt and the international lead investigator for the trial.

Asthma—a condition that affects the lung's airways and makes it hard to breathe—is the most common chronic disorder of childhood, with more than 5 million children under age 18 affected, according to the Centers for Disease Control and Prevention. It is a leading cause of hospitalization for children, and children with moderate-to-severe asthma may have reduced lung function and be at greater risk for lung diseases in adulthood, said Bacharier, who holds the Janie Robinson and John Moore Lee Chair in Pediatrics at Vanderbilt University School of Medicine.

"As asthma gets increasingly severe, the burden becomes substantial, impacting the child and the entire family," he said. "While we have very good asthma therapies available, none of them are perfect in eliminating severe exacerbations."

Dupilumab, a monoclonal antibody that targets type 2 inflammation, has been approved for the treatment of asthma in adults and adolescents for several years. Based on its established safety and efficacy, the investigators conducted a phase 3 clinical trial in 408 children between the ages of 6 and 11 who had uncontrolled moderate-to-severe asthma.

Children were randomized to receive a subcutaneous injection of dupilumab or placebo in addition to their standard therapy every two weeks for a year. Neither investigators nor participants knew who received active treatment versus placebo (double-blind trial design).

Most of the children in the trial had markers of type 2 inflammation, namely elevated levels of immune cells called eosinophils and/or elevated levels of nitric oxide in exhaled air. In patients with these markers, dupilumab significantly reduced the rate of severe exacerbations—symptoms requiring systemic steroid treatment, need for emergency care or hospitalization—by nearly 60%.

In addition, dupilumab improved lung function, measured by forced exhalation, and improved asthma control, assessed with standardized questionnaires administered by trained interviewers.

"This is the first study of its kind in children ages 6 to 11 that has demonstrated that a biologic improves asthma exacerbations, lung function and asthma control," Bacharier said. "We were not surprised, because dupilumab was very effective in clinical trials in adults and adolescents, but we were delighted with the results and the hope they bring to children and their families."

Dupilumab was not effective for the small number of children in the trial who did not have evidence of type 2 inflammation, consistent with expectations, he added.

The trial demonstrated that dupilumab was safe. Some children receiving active drug had increases in blood eosinophil levels or mild but manageable parasitic infections (type 2 immunity fights parasites), but very few participants had to discontinue dupilumab because of adverse reactions.

Patients in the VOYAGE trial were invited to join an extension trial for another year, with all participants receiving dupilumab. The extension trial will focus on both efficacy and long-term safety; results should be available in mid-2022.

Although two other biologic medicines targeting type 2 inflammation have been approved to treat asthma in children, neither has demonstrated improvements in all three key clinical endpoints—asthma exacerbations, lung function and asthma control—in a controlled clinical trial, Bacharier said.

Bacharier plans to explore the potential for dupilumab to modify asthma development. "Can we use this agent earlier in life to change how the disease develops? I think that's the next frontier," he said.

Bacharier is also a co-investigator of the PrecISE Network (Precision Interventions for Severe Asthma), a National Institutes of Health-funded network that is testing novel asthma therapies in patients with very severe asthma.

The Liberty Asthma VOYAGE trial (NCT02948959) was supported by Sanofi and Regeneron Pharmaceuticals, the manufacturers of dupilumab. Dupilumab is also FDA-approved for atopic dermatitis and chronic rhinosinusitis with nasal polyposis.

More information: Dupilumab in Children with Uncontrolled Moderate-to-Severe Asthma, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2106567

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