

Therapy for most common cause of cystic fibrosis safe and effective in 6-11

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An international, open-label Phase 3 study, co-led by Susanna McColley, MD, from Ann & Robert H. Lurie Children's Hospital of Chicago, found that a regimen of three drugs (elexacaftor/tezacaftor/ivacaftor) that targets the genetic cause of cystic fibrosis was safe and effective in 6-11-year-olds with at least one copy of F508del mutation in the CFTR gene, which is estimated to represent almost 90 percent of the cystic fibrosis population in the United States.

For children in this age group who have only one copy of F508del mutation—or about 40 percent of patients with cystic fibrosis in the United States—this would be the first treatment that addresses the underlying genetic defect in cystic fibrosis.

This three-drug cystic fibrosis treatment was approved by the FDA in October 2019 for people 12 years and older with at least one copy of F508del mutation. Based on the positive results of this study, the FDA has accepted the application to expand treatment indication to [younger children](#), with a decision expected by June 2021.

"The most exciting aspect of our findings is that this population of children had normal [lung](#) function at the start of the study and still had a significant improvement," said Dr. McColley, Co-Global Principal Investigator on the study and senior author, who is the Scientific Director for Interdisciplinary Research Partnerships at Stanley Manne Children's Research Institute at Lurie Children's and Professor of Pediatrics at Northwestern University Feinberg School of Medicine.

"Coupled with what we saw in studies and in practice with the older population, starting treatment earlier may avert serious long-term complications and really change the trajectory of health for children with cystic fibrosis."

Cystic fibrosis is a progressive genetic disease that damages multiple organs, including the lungs and pancreas. Currently, average life expectancy is 47 years. The disease is caused by [mutations](#) in the CFTR gene that lead to insufficient flow of salt and water in and out of cells. In the lungs, this creates buildup of thick, sticky mucus that can result in chronic lung infections and severe lung disease. Damage to the pancreas occurs even before birth, which interferes with nutrition absorption and growth. While there are approximately 2,000 known mutations of the CFTR gene, the most common is the F508del mutation.

In the 24-week study with 66 children, published in the *American Journal of Respiratory Care and Critical Care Medicine*, Dr. McColley and colleagues confirmed the appropriateness of a dose that is half of the adult daily dose of the three-drug treatment for children 6-11 years of age who weigh less than 30 kg and of the full adult dose for those weighing more. The regimen was well tolerated, and the safety profile was generally consistent with that observed in older patients, with cough, headache and fever as the most common adverse events.

The treatment resulted in significant improvements in lung function, respiratory symptoms and nutritional status. Maintaining or improving nutritional status is associated with better lung function and increased survival in patients with cystic fibrosis. In addition, substantial improvement in sweat chloride concentration, a direct measure of CFTR function, was observed.

"In this study, we saw greater improvements in sweat chloride than those previously seen in adults and adolescents," said Dr. McColley. "This

strong response to treatment may lead to better long-term clinical outcomes of cystic fibrosis."

"It's important to note that people with cystic [fibrosis](#) who are demographically characterized as having a race other than white or ethnicity characterized as Hispanic are less likely to have an F508del mutation," Dr. McColley said. "This is important because as with other acute and chronic conditions, these populations have more severe disease and lower life expectancy. As drug development continues, we are focused on having a highly effective treatment or cure for everyone with [cystic fibrosis](#)."

More information: Edith T. Zemanick et al, A Phase 3 Open-Label Study of ELX/TEZ/IVA in Children 6 Through 11 Years of Age With CF and at Least One F508del Allele, *American Journal of Respiratory and Critical Care Medicine* (2021). [DOI: 10.1164/rccm.202102-0509OC](https://doi.org/10.1164/rccm.202102-0509OC)

Provided by Ann & Robert H. Lurie Children's Hospital of Chicago

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