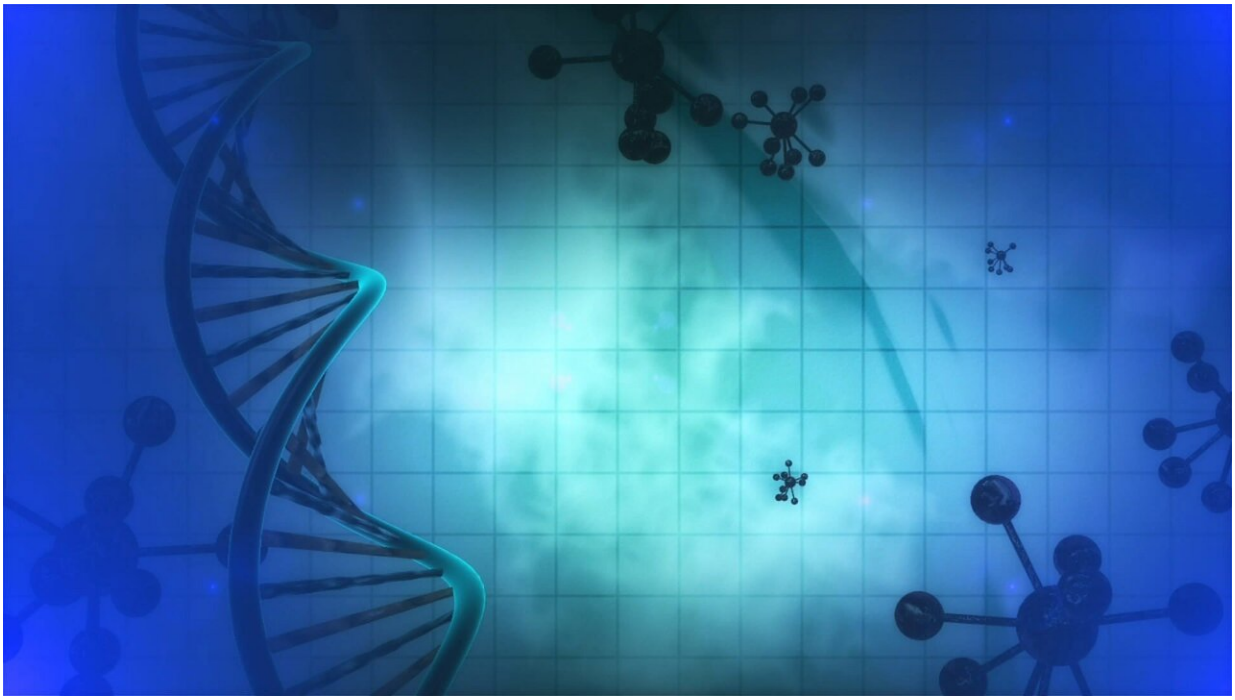
# New study determines cystic fibrosis therapy is safe and effective for young children

May 7 2021



Credit: CC0 Public Domain

Children ages two to five who have the most common form of cystic fibrosis (CF), caused by two copies of the F508 gene mutation, have not had any modulator treatments available to them until recently. A new study authored by researchers at Children's Hospital Colorado and published May 6, 2021, in *Lancet Respiratory Medicine* shows that the CFTR modulator—lumacaftor/ivacaftor—can be safe and well-tolerated

for this age range for up to 120 weeks, allowing younger children to begin proactive treatment of CF earlier in their lives.

CF affects more than 70,000 people worldwide and is a chronic, progressive, life-shortening genetic disease caused by an absent or defective protein called the CF transmembrane conductance regulator (CFTR) protein, resulting from mutations in both copies of the CFTR gene. Most people with CF have little to no CFTR protein function. CFTR modulators target the specific defects caused by mutations in the CFTR gene to increase the quantity or function of CFTR protein. Lumacaftor/ivacaftor is the first combination CFTR modulator therapy approved to treat people with CF who have two copies of the most common disease-causing CFTR mutation.

While a prior study found that up to 24 weeks of lumacaftor/ivacaftor was safe and effective, the safety and efficacy of long-term lumacaftor/ivacaftor treatment had not previously been investigated in children under the age of six. During this new study, 57 children between two and five years of age received weight- and age-based doses of lumacaftor/ivacaftor every 12 hours for over 96 weeks with the end results demonstrating that lumacaftor/ivacaftor is safe, effective and can be used for up to 120 weeks of treatment.

"Starting CFTR modulator treatments at a younger age may help to slow and hopefully prevent some of the devastating consequences of CF, such as lung damage, lung function decline and frequent illnesses or hospitalizations," said lead study author Jordana Hoppe, MD, a pediatric pulmonologist with Children's Hospital Colorado and assistant professor of pediatrics at the University of Colorado School of Medicine on the Anschutz Medical Campus. "Prior to the approval of lumacaftor/ivacaftor for children between 2-5 years old, younger patients with two copies of the F508 mutation could only receive symptomatic treatments such as manual chest percussion to clear mucus

from the airways, nebulized treatments or antibiotics. The modulator therapy is preventive instead of reactive, targeting the function of the protein to make it work better."

Another key finding demonstrated improvements or an increase in pancreatic function. CF can cause pancreatic insufficiency so that those with the disease must ingest pancreatic enzymes every time they eat to maintain growth and nutrition. These results suggest that for some patients treated with the CFTR modulator therapy, there may be improvement in pancreatic function, possibly resulting in changes to their enzyme dosing.

Additional results included changes in sweat chloride, improved weight gain and growth, and increased lung clearance. It also helps prevent pulmonary exacerbations or respiratory illnesses that require hospitalizations and antibiotic therapy, which has been especially alleviating for families during the COVID-19 pandemic.

"These patients will be transitioned to a more highly effective modulator TRIKAFTA*, but there are certainly benefits to starting modulator therapy at a younger age as the results of this study demonstrated," Hoppe said.

Study visits were conducted in the Colorado Clinical and Translational Sciences Institute (CCTSI) research area at Children's Hospital Colorado. The hospital's Mike McMorris Cystic Fibrosis Research and Care Center is the largest center of its kind in the nation and follows close to 400 children.

"The Colorado Clinical and Translational Sciences Institute (CCTSI) has been a longtime partner with the Mike McMorris Cystic Fibrosis Research and Care Center. Our pediatric Clinical and Translational Research Center and our specialized research nursing staff assist the CF

investigators like Dr. Hoppe with conducting CF clinical trials in many ways, including collecting data and obtaining specimens, infusing medications and educating the families and children about research," said Ronald Sokol, MD, director of the CCTSI and vice chair of pediatrics at Children's Hospital Colorado.

*In 2019, researchers at the Children's Hospital Colorado Breathing Institute, one of the largest CF clinical care centers in the U.S., were part of a Therapeutics Development Network that oversaw clinical trials leading to FDA approval of TRIKAFTA, a highly effective CF treatment for people with CF 12 years of age and older. The team was also involved in trials of TRIKAFTA in children ages 6-11 years, which was recently proven efficacious for this patient population and could be soon approved by the FDA for use for kids 6 and older. TRIKAFTA is a combination of three medicines that can improve the CFTR protein function to over 50%, helping approximately 90% of people living with CF.

**More information:** Jordana E Hoppe et al, Long-term safety of lumacaftor–ivacaftor in children aged 2–5 years with cystic fibrosis homozygous for the F508del-CFTR mutation: a multicentre, phase 3, open-label, extension study, *The Lancet Respiratory Medicine* (2021). DOI: 10.1016/S2213-2600(21)00069-2

Provided by Children's Hospital Colorado