Cystic Fibrosis Research News

Title:
Effects of Ivacaftor on Systemic Inflammation and the Plasma Proteome in People with CF and G551D

Lay Title:
How ivacaftor changes inflammation and protein levels in the bloodstream of people with CF and the G551D mutation

Authors:
Jordana E. Hoppe[1], Brandie D. Wagner[2], J. Kirk Harris[1], Steven M. Rowe[3], Sonya L Heltshe[4], Emily M. DeBoer[1], Scott D. Sagel[1]

Affiliations:
[1]Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, CO
[2]Department of Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO
[3]Department of Medicine, Pediatrics and Cell Developmental and Integrative Biology, University of Alabama Birmingham, Birmingham, AL
[4]Department of Pediatrics, University of Washington, Cystic Fibrosis Foundation Therapeutics Development Network Coordinating Center, Seattle, WA

What was your research question?
We wanted to better understand how ivacaftor, a highly effective *CFTR* modulator, causes changes in inflammation and other organ systems throughout the entire body. We did so by measuring proteins in the bloodstream of people with CF and the G551D *CFTR* genetic change.

Why is this important?
While we know that ivacaftor treatment improves lung function, reduces symptoms and the frequency of respiratory illnesses, we do not fully know how this medicine affects inflammation, an important cause of lung damage in CF, or other parts of the body, outside of the lungs. Changes in proteins in the bloodstream may help us to better understand why people with CF grow better on this medication and why they report less respiratory and digestive symptoms and more mental health symptoms (feeling sad or anxious). These proteins could serve as biomarkers, indicators of how the body is responding to ivacaftor treatment.

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What did you do?

We measured inflammatory and growth-related proteins in blood samples from 64 children and adults with CF before starting ivacaftor treatment and 1 and 6 months after starting treatment. In a second group of 30 people with CF, we looked at over 1,300 proteins at the same time in blood collected before and 6 months after starting ivacaftor using a special technology. We also looked at how changes in many of these proteins related to changes in clinical improvements including lung function, body mass index and sweat chloride measurements with ivacaftor treatment.

What did you find?

Ivacaftor treatment led to a decrease in a few proteins that are part of the body's inflammatory response and an increase in a protein that affects height. Of the over 1,300 proteins measured in the second group, 9 changed significantly with ivacaftor. Some of these proteins are made in or have effects in the pancreas and the brain and central nervous system. Other proteins are involved in fat digestion and how cells are organized. Changes in several proteins were related to improvements in lung function, weight and sweat chloride measurements.

What does this mean and reasons for caution?

This study suggests that 6 months of ivacaftor lessens inflammation in the body, and improves protein absorption, along with fat absorption, in the intestines. Importantly, changes in several proteins indicate that ivacaftor affects multiple organs in the body including the pancreas and central nervous system. These findings may lead to more research to try to answer how inflammation is decreased or how other organs in the body work following ivacaftor treatment. This study does not show how ivacaftor changes inflammation in the lung (for example, in mucus).

What's next?

We want to know whether similar changes in inflammation, digestion, and growth are seen with the triple combination *CFTR* modulators. We also want to learn what changes in proteins in the bloodstream are seen in younger children with CF (< 6 years of age) who are treated with *CFTR* modulators.

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cfresearchnews@gmail.com