European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

The effect of discontinuing hypertonic saline or dornase alfa on mucociliary clearance in elexacaftor/tezacaftor/ivacaftor treated people with cystic fibrosis: The SIMPLIFY-MCC Study

Lay Title:

Effect of stopping inhaled therapies on mucus clearance while on elexacaftor/tezacaftor/ivacaftor

Authors:

Scott H. Donaldson[1], Timothy E. Corcoran[2], Joseph M. Pilewski[2], Beth L. Laube[3], Peter Mogayzel[3], Agathe Ceppe[1], Jihong Wu[1], Kirby Zeman[1], Steven M. Rowe[4], David P. Nichols[5], Alex H. Gifford[6], William D. Bennett[1], Nicole Mayer-Hamblett[5], on behalf of the SIMPLIFY MCC Study teams.

Affiliations:

[1] Department of Medicine and the Marsico Lung Institute, University of North Carolina at Chapel Hill, Chapel Hill, NC
[2] Department of Medicine, University of Pittsburgh, Pittsburgh, PA
[3] Department of Pediatrics, Johns Hopkins University, Baltimore, MD
[4] Department of Medicine and the Gregory Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham, Birmingham, AL
[5]Seattle Children's Research Institute, Seattle, WA and Dept of Pediatrics, University of Washington, Seattle, WA
[6]University Hospitals Cleveland Medical Center and University Hospitals Rainbow Babies and Children's Hospital, Cleveland, OH

What was your research question?

Will stopping hypertonic saline (HS) or dornase alfa (DA) cause mucus clearance to deteriorate in people with CF taking elexacaftor/tezacaftor/ivacaftor (ETI)?

Why is this important?

People with CF treated with ETI often have better lung function and fewer respiratory symptoms. In this setting, the ongoing need for other time-consuming inhaled treatments to maintain lung health is uncertain. The ability to safely stop HS and/or DA treatments would provide significant time and cost savings and should improve patient's quality of life.

Cystic Fibrosis Research News

What did you do?

The SIMPLIFY-MCC Sub-study was conducted as part of the larger SIMPLIFY Study. In this study, participants with CF ≥12 years of age were randomly assigned to either continue or stop using either hypertonic saline or dornase alfa, depending upon what they had been using before the trial. Measurement of mucus clearance rates, with a technique that uses inhaled radioactive particles, was made before and 6 weeks later. Lung function and symptoms were also measured. Seventeen participants each were enrolled into the HS and dornase alfa study arms.

What did you find?

Enrolled participants into each study had mild lung disease at baseline. In the HS study, mucus clearance rates did not drop after stopping treatment, and there was no difference in mucus clearance, lung function, or symptoms between those that continued or stopped treatment. In the DA study, mucus clearance rates improved significantly after stopping treatment, whereas no change was observed in those that continued DA. No differences in lung function or symptoms were observed between the groups that stopped or continued DA.

What does this mean and reasons for caution?

In patients with mild lung disease, it appears safe to discontinue either HS or DA, at least over a 6-week period, with no deterioration in mucus clearance rates, lung function, or symptoms. Improved mucus clearance after stopping DA was a surprising finding. It is uncertain, however, whether greater deterioration in health could occur over longer periods after stopping these treatments, and those with more severe lung disease cannot expect the same results and should be cautious.

What's next?

We await results of ongoing research describing the impact of longer periods of treatment discontinuation in people with CF. Additional research into the need for existing and new therapies in people with CF treated with ETI, particularly in those with more severe disease, is needed.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/38355350/

cfresearchnews@gmail.com