Cystic Fibrosis Research News

Title:

The clinical effectiveness of elexacaftor/tezacaftor/ivacaftor (ETI) for people with CF without a F508del variant: A systematic review and meta-analysis

Lay Title:

Evaluating the Effectiveness of a Novel CF Medication for People Without Common Cystic Fibrosis-causing Genetic Mutations

Authors:

Daniel Lupas[a], Frank Y. Chou[c], Mohammad Abdullah Al Hakani[d], Ishita Kuthiala[a], Arjuna Srikrishnaraj[a], Xuan Li[b], Naomi Potter[b], Bradley S. Quon[b,c]

Affiliations:

[a] Schulich School of Medicine, Western University, London, Ontario, Canada
[b] Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada
[c] Division of Respiratory Medicine, Department of Medicine, University of British Columbia, Vancouver, BC, Canada
[d] Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

What was your research question?

Elexacaftor/tezacaftor/ivacaftor (ETI) is a medication approved to treat people with Cystic Fibrosis (pwCF) who have the F508del genetic variant. We wanted to assess whether this medication is also effective for people with CF who do not have the F508del genetic variant.

Why is this important?

Cystic fibrosis is a rare genetic condition that primarily affects the lungs and digestive system among other organs. The F508del mutation is the most prevalent CF-causing variant worldwide. ETI has been shown to improve lung function and reduce symptoms in pwCF with F508del; however, its effectiveness in patients with other genetic variants that cause CF is not well understood. Given that a significant number of pwCF do not carry the F508del variant, it is of interest to determine if ETI can also help these individuals.

What did you do?

We conducted a systematic review and meta-analysis, which means that we carefully searched and analyzed all available studies on this topic. Our search spanned multiple medical databases and included data from January 1, 2019 to May 14, 2024. Studies of interest

included those that reported the clinical response to ETI in pwCF without the F508del variant. We analyzed the data across multiple studies to see how ETI affected lung function and sweat chloride levels.

What did you find?

Our search revealed 20 studies that met our criteria and were included in our analysis. Within these studies, data from 164 patients were extracted and a total of 120 (73%) showed a positive clinical response to ETI. This was defined by a significant improvement in lung function or a decrease in sweat chloride levels. We found 51 unique CF-causing genetic mutations among those who responded to treatment, 27 of which had not been previously approved by the U.S. Food and Drug Agency (FDA) for ETI treatment.

What does this mean and reasons for caution?

Our results suggest that ETI is effective in improving the health of pwCF without the common F508del variant. Ultimately, this may lead to expanded use of ETI providing more patients with effective treatment options. It is important to recognize, however, that additional research is needed to confirm some of our findings particularly as only one or a few individuals were treated with ETI for some variants to assess clinical response. Our study also includes data from various sources that utilized different study designs.

What's next?

Future efforts would benefit from controlled clinical trials to verify ETI effectiveness in this population. Moreover, as the evidence continues to evolve rapidly, we propose the development of a publicly available database to better track this data in real time. This research will support regulatory approval and broader access to ETI, improving treatment and quality of life for more pwCF.

Original manuscript citation in PubMed

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cfresearchnews@gmail.com