European Cystic Fibrosis Society

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

Cystic Fibrosis Research News

Title:

Tezacaftor/ivacaftor in people with cystic fibrosis who stopped lumacaftor/ivacaftor due to respiratory adverse events

Authors:

Carsten Schwarz[a], Sivagurunathan Sutharsan[b], Ralph Epaud[c], Ross C. Klingsberg[d], Rainald Fischer[e], Steven M. Rowe[f], Paul K. Audhya[g], Neil Ahluwalia[h], Xiaojun You[g], Thomas J. Ferro[g], Margaret E. Duncan[h], Bote G. Bruinsma[h]

Affiliations:

[a]Christiane Herzog Zentrum Berlin/Charité–Universitätsmedizin Berlin, Berlin, Germany;
[b]Division of Cystic Fibrosis, Department of Pulmonary Medicine, Faculty of Medicine, Universitat Duisburg Essen–Ruhrlandklinik, Essen, Germany;
[c]Cystic Fibrosis and Rare Lung Disease Centre, Centre Hospitalier Intercommunal de Créteil, Créteil, France;
[d]Tulane University School of Medicine, New Orleans, LA, United States;
[e]Pneumologische Praxis München-Pasing, Munich, Germany;
[f]The University of Alabama at Birmingham, Birmingham, AL, United States;
[g]Formerly of Vertex Pharmaceuticals Incorporated, Boston, MA, United States;
[h]Vertex Pharmaceuticals Incorporated, Boston, MA, United States

What was your research question?

Is tezacaftor/ivacaftor safe and does it work well in people 12 years of age or older who (1) have 2 copies of a mutation called Phe508del in the *CFTR* gene, (2) had respiratory side effects after taking lumacaftor/ivacaftor, and (3) stopped taking lumacaftor/ivacaftor because of these side effects?

Why is this important?

Lumacaftor/ivacaftor was the first of a type of medicine called “CFTR modulator combination therapy” that was approved to treat people 12 years of age or older who have cystic fibrosis and 2 copies of the Phe508del-*CFTR* mutation. Some people with more severe lung disease have opted to stop taking lumacaftor/ivacaftor due to respiratory side effects. Tezacaftor/ivacaftor is another combination therapy that these patients may be able to take. This study looked at whether tezacaftor/ivacaftor treatment is safe and works well so that these patients may benefit from treatment for their underlying cystic fibrosis disease.

Cystic Fibrosis Research News

What did you do?

The study included people 12 years of age or older with cystic fibrosis who have 2 copies of the Phe508del-*CFTR* mutation and who previously stopped taking lumacaftor/ivacaftor because of respiratory side effects. They were given either tezacaftor/ivacaftor (tezacaftor 100 mg/ivacaftor 150 mg in the morning and ivacaftor 150 mg in the evening) or placebo (inactive medicine) for 56 days. After the people stopped taking the treatments, they were checked for another 28 days. Researchers looked at how many people reported certain respiratory side effects during the study. Changes in lung function and other safety measures were also evaluated.

What did you find?

14.0% of people who took tezacaftor/ivacaftor and 21.3% of people who took placebo experienced respiratory side effects. All of the respiratory side effects, such as shortness of breath or chest tightness, were mild or moderate and none caused the people taking part to stop or interrupt the treatment. Researchers did not see any new concerns about the safety of tezacaftor/ivacaftor. People taking tezacaftor/ivacaftor had improvements in their lung function by an average of 2.7 percentage points more than people taking placebo.

What does this mean and reasons for caution?

The results of this study suggest that people aged 12 years or older with cystic fibrosis and 2 copies of the Phe508del-*CFTR* mutation who could not take lumacaftor/ivacaftor treatment because of respiratory side effects can safely take tezacaftor/ivacaftor. These people may also experience benefits from taking tezacaftor/ivacaftor, such as better lung function. This study was only 8 weeks long, so it did not look at long-term effects. But with lumacaftor/ivacaftor, respiratory side effects usually happened in the first few weeks of treatment, so 8 weeks of tezacaftor/ivacaftor treatment should be long enough for researchers to see any side effects.

What's next?

Tezacaftor/ivacaftor is part of a combination of 3 medicines, elexacaftor/tezacaftor/ivacaftor, that was recently approved to treat people with cystic fibrosis 12 years of age or older with 1 copy of the Phe508del-*CFTR* mutation. This study supports using elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis who experienced respiratory side effects with lumacaftor/ivacaftor.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/32586736/

cfresearchnews@gmail.com

Cystic Fibrosis Research News