Cystic Fibrosis Research News

Title:

Regarding the article entitled "Effect of elexacaftor/tezacaftor/ivacaftor on annual rate of lung function decline in people with cystic fibrosis"

Lay Title:

A letter in response to the recently published article entitled "Effect of elexacaftor/tezacaftor/ivacaftor on annual rate of lung function decline in people with cystic fibrosis"

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What was your research question?

We wrote a letter in response to an article published in the Journal of Cystic Fibrosis (CF) by Lee and colleagues. This article was focused on the effect of a new CF drug treatment (elexacaftor/tezacaftor/ivacaftor) on lung function (measure of how well someone's lungs are working) in people with CF.

Why is this important?

In their study, Lee and colleagues concluded that a new medication (elexacaftor/tezacaftor/ivacaftor, or Trikafta®) is the first CF treatment that halts lung function decline over a two-year follow-up period. However, we think there are some other factors that the authors of the published study had not considered or may have underestimated in highlighting the positive effect of the new medication. Not considering these factors may overestimate the positive impact that Trikafta® has on lung function in CF,

which may be misleading for the CF community. We wrote a research letter to highlight the other factors that should perhaps be considered.

What did you do?

We have read other papers related to the effect of Trikafta® on lung function in CF. The paper published in the Journal of Cystic Fibrosis (CF) by Doumit and colleagues points that it is possible for lung function to improve during the Covid-19 lockdown, even among people with CF not on Trikafta®. The paper published in the American Journal of Epidemiology by Newsome and colleagues points out the potential bias in estimating effects of treatment using comparison against historical data. Newsome and colleagues recommend using statistical analysis that considers both historical and contemporary control groups.

What did you find?

Lee and colleagues looked at participants aged ≥12 years who received Trikafta® in clinical trials over a two-year period (2018/2019 to 2020/2021). They compared these participants with 2012-2017 data collected from the US CF Foundation Patient Registry (before the new medication was available). The US Covid-19 lockdown started in March 2020. This means that some of the lung function data from drug-treated participants (depending on when participants joined the trials) was collected when people with CF were shielding and may have been exposed to fewer bugs, hence there may be fewer chest flare-ups and improved lung function even without Trikafta®.

What does this mean and reasons for caution?

A study by Doumit and colleagues highlighted the lung function improvement seen during the Covid-19 lockdown among people with CF largely not on Trikafta®. If the results of the Doumit study can be generalised to other people with CF, this suggests that people with CF not on Trikafta® may also have improved lung function over the same time period as the participants receiving Trikafta®. Since only participants receiving Trikafta® had some of their lung function data collected during Covid-19 lockdown, this may bias the Lee results in favour of the participants receiving Trikafta® by overestimating the effects on lung function.

What's next?

Instead of comparing groups over different time periods using historical data, there may be other more appropriate methods to estimate the effect of Trikafta®. The lung functions of people on Trikafta® should be monitored over a longer time period, especially as people with CF start returning to their pre-pandemic lifestyles.

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