

# Cystic Fibrosis Research News

**Title:**

TREATMENT EFFECTS OF ELEXACAFTOR/TEZACAFTOR/IVACAFTOR IN PEOPLE WITH CF CARRYING NON-F508DEL MUTATIONS

**Lay Title:**

The effects of Trikafta/Kaftrio on people with CF who have mutations other than the most common CF mutation (F508del)

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**What was your research question?**

CF is caused by several hundred "mutations"- changes in the CF gene that cause abnormal function. Trikafta (Kaftrio) was tested on people who have the most common CF mutation called F508del. We report the results of treatment with Trikafta in people who have CF with mutations other than F508del.

**Why is this important?**

Several of the mutations that cause CF may be corrected with Trikafta according to studies in the laboratory. Because these mutations are very rare, clinical trials (which test the effects of

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a drug on a group of people) were performed only in people with CF who have the most common mutation, F508del. Clinical trials were not done people with CF mutations other than F508del, and so the actual effects on people with CF are unknown. Some countries agree to authorise and pay for the treatment only if it was proven to help people (for example in clinical trials).

## What did you do?

In Israel, Trikafta is provided for patients if they have CF mutations which have been shown by studies in the lab to improve with treatment, even if clinical trials were not done. We invited all CF centers in Israel to report the experiences of treating people with CF and mutations other than F508del. We asked to include people who were treated with Trikafta for at least three months, and documented sweat test, lung function, weight, and need for antibiotics before starting Trikafta, and after 3-6 months with treatment.

## What did you find?

Sixteen people with CF were treated with Trikafta. Eight did not receive CF specific drugs (called “modulators”) previously, another eight were switched to Trikafta from Kalydeko or Symdeko (Symkevi). In the eight patients without previous treatment, there were significant improvements in sweat test and need for antibiotics compared to before treatment: On treatment, people did not have periods of worsening (“exacerbations”) while most people had 1.5 exacerbations in the year before starting treatment. Lung function also improved from an average of 66.3% to 72.4%. The people who were previously treated with Kalydeko or Symdeko did not improve further on Trikafta.

## What does this mean and reasons for caution?

We show that in people with CF and certain rare mutations other than F508del, treatment with Trikafta has important health benefits. This may not be attributable to all patients because only people who have certain mutations that have been authorised for Trikafta received treatment. People who have received previous treatment with other drugs may still improve by switching to Trikafta- but because of the small number of patients, the patients in our study may have not improved due to chance; other people may improve with treatment. We did not record symptom improvement, which is very important to people with CF.

## What’s next?



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There are other CF mutations that may improve with Trikafta and other existing modulators or such that will become available in the future. We suggest that when clinical trials cannot be done, information on treatment of people is collected and reported.

## **Original manuscript citation in PubMed**

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