



Cystic Fibrosis Research News

Title:

EFFECT OF ELEXACAFTOR-TEZACAFTOR-IVACAFTOR ON BODY WEIGHT AND METABOLIC PARAMETERS IN ADULTS WITH CYSTIC FIBROSIS

Lay Title:

Effects of CFTR Modulators on Metabolic Parameters

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What was your research question?

Several months after the widespread introduction of elexacaftor-tezacaftor-ivacaftor in adult patients with CF, a trend towards increased weight was apparent in our clinic. To further analyze this, we systematically reviewed changes in weight, blood pressure, and other markers of metabolic health over the first 12 months of elexacaftor-tezacaftor-ivacaftor (ETI) therapy.

Why is this important?

People with CF have historically had lower-than-average body weight for age. Being underweight is associated with worse respiratory function, and weight gain has historically been a point of emphasis for clinicians and patients with CF.

Because of its beneficial effect on lung function and respiratory symptom burden, the combination CFTR modulator therapy elexacaftor-tezacaftor-ivacaftor (brand name Trikafta) was approved in late 2019 in the United States for patients with CF carrying at least one delta F508 mutation. ETI was associated with weight gain in clinical trials, but no real-world data describing the effect of ETI on weight and metabolic health have yet been published.

What did you do?

Of 200 adult patients in the University CF clinic, 134 were eligible for inclusion in the study. We collected data on each person's body weight, body mass index (BMI), and blood pressure

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at each clinic visit for the year before elexacaftor-tezacaftor-ivacaftor was started and the year after. We compared each person's weight trajectory in the year before starting elexacaftor-tezacaftor-ivacaftor to their weight trajectory in the year after starting ETI. We considered the difference in weight trajectories to represent the effect of elexacaftor-tezacaftor-ivacaftor.

What did you find?

Elxacaftor-tezacaftor-ivacaftor was associated with weight gain of about 4 kilograms (8.8 lbs). After a year of ETI, less patients at our center were underweight (7.5% before, 2.2% after) and more were overweight (19.4% before, 31.3% after) or obese (7.5% before, 9.7% after). ETI-associated increase in weight occurred regardless of patient sex, genotype, prior CFTR modulator use, CF-related diabetes (CFRD) status, or CF-related hospitalization during the study period.

Blood pressure also rose on ETI, with percentage of patients with hypertension (high blood pressure) increasing from 35% before ETI to 63% after.

Finally, other blood tests reflecting metabolic health were reviewed. For patients without CFRD, blood sugars and hemoglobin A1c (a 3 month blood sugar average) improved on elxacaftor-tezacaftor-ivacaftor. For patients with CFRD, there was no effect of ETI on A1c, however, these patients exhibited significant increases in cholesterol.

What does this mean and reasons for caution?

Overall, our findings indicate that elxacaftor-tezacaftor-ivacaftor tends to increase body weight and blood pressure, and may affect other markers of metabolic health.

What's next?

This highlights the need for individualized nutritional and lifestyle counseling for people with CF to avoid the harmful effects of overnutrition, such as obesity, hypertension, and high blood lipids. Further research is needed to delineate the most optimal ways to screen for and treat these conditions.

Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/34862121/>