

Cystic Fibrosis Research News

Title:

Elexacaftor/tezacaftor/ivacaftor and mental health: A workshop report from the Cystic Fibrosis Foundation's Prioritizing Research in Mental Health Working Group

Lay Title:

A review of research about Trikafta and mental health: a report from Cystic Fibrosis Foundation's Prioritizing Research in Mental Health Working Group

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What was your research question?

What is currently known about Trikafta and its impact on mental health? Where are the critical gaps in knowledge?

Cystic Fibrosis Research News

Why is this important?

Mental health is one of the top priorities for the cystic fibrosis (CF) community. Because of this, the CF Foundation created a working group dedicated to mental health research called *Prioritizing Research in Mental Health* (PRIME). PRIME consists of CF academic researchers and community members. Its first priority is trying to understand the relationship between mental health and Trikafta.

What did you do?

PRIME reviewed existing literature about Trikafta and mental health in several areas:

- Laboratory studies
- Studies of how Trikafta is processed by the body, and whether Trikafta blood levels are related to side effects
- Changes in mood and anxiety
- Impact on quality of life and self-image
- Cognitive symptoms after starting Trikafta, such as brain fog, trouble with concentration, poor memory
- Changes in sleep
- Management of new or worsening mental health symptoms

What did you find?

Most people with CF (PWCF) experience improved quality of life and well-being after beginning Trikafta. However, a subset has had new or worsening mental health symptoms. These include depression, anxiety, behavior change, sleep disturbance, cognitive symptoms, and negative impact on body image.

Little is known about why some people experience these symptoms after starting Trikafta. CFTR (the protein causing CF) is found in parts of the brain that influence mood and cognition. We don't know what the impact is on the brain when Trikafta changes how CFTR works. Individual reports describe that changing doses or stopping Trikafta sometimes improves these symptoms.

What does this mean and reasons for caution?

Most of this data comes from observations of PWCF describing their experiences and symptoms. There is a need for studies that include a large number of participants who are followed for multiple months to collect data about changes in their mental health. These



Cystic Fibrosis Research News

studies need to include reliable measures to fully evaluate the impact of Trikafta on mental health.

To help us understand how to improve mental health symptoms, we need more research on how Trikafta affects the brain and nervous system. This includes studies of whether medication levels in the blood are associated with changes in mental health.

What's next?

PRIME members are collaborating on multiple studies specifically looking at CFTR modulators and mental health, including designing a study to monitor the impact of the newest CFTR modulator, vanzacaftor/tezacaftor/deutivacaftor (the “vanza triple”), on PWCF who had stopped or modified their dose of Trikafta due to mental health symptoms.

Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/39592379/>