**Title:**

LONGITUDE: An observational study of the long-term effectiveness of elexacaftor/tezacaftor/ivacaftor in people aged ≥12 years with cystic fibrosis using data from the United Kingdom Cystic Fibrosis Registry - 2-year analysis

**Lay Title:**

From Clinical Trials to Real Life: Impact of Elexacaftor/Tezacaftor/Ivacaftor in the United Kingdom

**Authors:**

Gabriela Vega-Hernandez,a Gordon MacGregor,b Andrew Wilfin,a Francis Adams,c Ciarán Haugh,c Carl A. Baxter,a Heike Wöhling,d Sarah L. Clarke,c Susan C. Charman,c Siobhán B. Carre

**Affiliations:**

aVertex Pharmaceuticals Incorporated, London,

bDepartment of Respiratory Medicine, NHS Greater Glasgow and Clyde, Queen Elizabeth University Hospital, Glasgow, UK

cCystic Fibrosis Trust, London, UK

dVertex Pharmaceuticals (Germany) GmbH, Munich, Germany

eRoyal Brompton Hospital, part of Guy’s and St Thomas’ NHS Foundation Trust and NHLI, Imperial College, London, UK

**What was your research question?**

Everyone has a protein in their cells called cystic fibrosis transmembrane conductance regulator (CFTR) that helps move salt and water in and out of cells, keeping mucus thin and slippery. In people with cystic fibrosis (CF), this protein does not work properly, leading to thick, sticky mucus that clogs the lungs and other organs. Scientists developed medicines called CFTR modulators that help this protein work better. Elexacaftor/tezacaftor/ivacaftor is a CFTR modulator medicine that led to improvements in lung function, nutrition, frequency of respiratory illness, and respiratory symptoms when tested in clinical trials of people with CF. We asked how well elexacaftor/tezacaftor/ivacaftor works in everyday life.

**Why is this important?**

Clinical trials test the safety and effectiveness of medicines in carefully controlled conditions. Real-world studies help confirm that the benefits seen in clinical trials happen in everyday life. Confirmation of clinical trial results in the real world helps doctors, patients, and health systems feel more confident that elexacaftor/tezacaftor/ivacaftor can improve and extend the lives of people living with CF.

**What did you do?**

Elexacaftor/tezacaftor/ivacaftor is an approved medication in the United Kingdom (UK) for people with CF. We used information from the UK CF Registry, which holds health data from people with CF, to look at data from over 5000 people, 12 years of age and older, who started taking elexacaftor/tezacaftor/ivacaftor. We looked at how these people on elexacaftor/tezacaftor/ivacaftor did before and after (for 1 or 2 years) they started the medication and also compared them with others who never took a CFTR modulator medicine. We looked to understand how well their lungs worked, their weight, how often they got lung infections or needed extra treatment, if they needed lung transplants, how long they were living, and if they stopped taking elexacaftor/tezacaftor/ivacaftor.

**What did you find?**

We learned that 60% of people were taking a different CFTR modulator medicine before switching to elexacaftor/tezacaftor/ivacaftor. People who were not taking any CFTR modulator medicine lost lung function faster over time, which could lead to serious health problems and early death. In contrast, people who took elexacaftor/tezacaftor/ivacaftor for 1 or 2 years had improved lung function. Many people had healthier weight, which is important for staying strong. People were getting less sick, and lung infections went down by 65%, meaning people did not need strong antibiotics as often. Because this medicine helps lung function, fewer people needed lung transplants and fewer people died. Lastly, very few people (4%) stopped taking the medicine.

**What does this mean?**

The findings from this study confirm that elexacaftor/tezacaftor/ivacaftor is beneficial in real life. These data show that elexacaftor/tezacaftor/ivacaftor is making an impactful difference for people with CF, helping them breathe better, improving their overall health, and reducing serious disease complications.

**What’s next?**

Scientists will continue to study CF treatments, including elexacaftor/tezacaftor/ivacaftor, to understand how they affect the lives of people with CF.

**Original manuscript citation in PubMed**

<https://pubmed.ncbi.nlm.nih.gov/40379539/>