

Cystic Fibrosis Research News

Title:

TEZACAFTOR/IVACAFTOR IN PEOPLE WITH CYSTIC FIBROSIS HETEROZYGOUS FOR MINIMAL FUNCTION *CFTR* MUTATIONS

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What was your research question?

Is tezacaftor/ivacaftor, a *CFTR* modulator combination, safe and does it work well to treat people ≥ 12 years old with cystic fibrosis (CF) who carry one *F508del-CFTR* mutation and another *CFTR* mutation called a minimal function (MF) mutation?

Why is this important?

Therapy with tezacaftor/ivacaftor has been shown to work and be safe in people ≥ 12 years old with CF who are homozygous for *F508del-CFTR* or heterozygous for *F508del-CFTR* and another *CFTR* mutation called a residual function mutation. To date no studies have looked at whether tezacaftor/ivacaftor is also safe and works to treat people ≥ 12 years old with CF who are heterozygous for *F508del-CFTR* and a MF mutation, which represents a large proportion of the CF population ($\approx 30\%$). At the time this study was done, no *CFTR* modulators had been approved to treat people with these mutations.

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What did you do?

In this Phase 3, randomized, double blind, placebo-controlled, multicenter study, people ≥ 12 years old with CF who were heterozygous for *F508del-CFTR* and a MF mutation received tezacaftor/ivacaftor for 12 weeks. We looked at how safe the drug was, how well it worked, and whether people taking the drug could tolerate it. This study planned to enroll about 300 people. An interim analysis to determine whether the study should continue enrolling participants was planned when about half of the participants had finished 12 weeks of treatment. Enrollment was paused when 168 people were enrolled.

What did you find?

We found that tezacaftor/ivacaftor therapy did not significantly improve lung function or any of the other measures of health that were studied in people ≥ 12 years old with CF who were heterozygous for *F508del-CFTR* and a MF mutation. Therefore, as tezacaftor/ivacaftor did not work well in this group of people, the study was terminated early. However, tezacaftor/ivacaftor was generally safe, and well tolerated, which has been shown in other studies of tezacaftor/ivacaftor in people ≥ 12 years old with CF.

What does this mean and reasons for caution?

The results of this study show that people with a single *F508del-CFTR* mutation and a MF mutation did not get clinical benefit from treatment with tezacaftor/ivacaftor. Thus, the study sponsor did not seek approval for tezacaftor/ivacaftor to be used to treat people with CF who are heterozygous for the *F508del-CFTR* mutation and a MF mutation.

What's next?

In recent trials, adding the corrector elexacaftor to tezacaftor/ivacaftor demonstrated clinical benefit in people with CF heterozygous for *F508del-CFTR* and a MF mutation. Elexacaftor/tezacaftor/ivacaftor was generally safe and well tolerated; it is approved in the United States to treat people ≥ 12 years old with CF with ≥ 1 copy of *F508del-CFTR*.

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