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Title:

EMPIRE-CF STUDY: A PHASE 2 CLINICAL TRIAL OF LEUKOTRIENE A4 HYDROLASE INHIBITOR ACEBILUSTAT IN ADULT SUBJECTS WITH CYSTIC FIBROSIS

Lay Title:

STUDY THAT TESTED THE EFFECTS OF A NEW DRUG CALLED ACEBILUSTAT IN ADULTSWITH CYSTIC FIBROSIS

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What was your research question?

Researchers wanted to know 1) how effective would acebilustat be in improving lung function in people with CF, 2) whether acebilustat would be a safe treatment in people with CF, and 3) whether acebilustat would help prevent worsening of respiratory symptoms, also known as pulmonary exacerbations, in people with CF.

Why is this important?

People with CF suffer from inflammation, which occurs due in part to a high level of cells called neutrophils in their airways. These cells aggravate the airway damage and worsen a person's health. Researchers have observed that one way to reduce the harmful effects of neutrophils might be to change the function of molecules in the body that activate the neutrophils. Acebilustat blocks the body from making one of these molecules, called leukotriene B4 (LTB_4). People with CF who benefit from CFTR modulator therapies still have exacerbations and lose lung function over time. Therefore, additional types of treatments are needed which makes studying acebilustat relevant.

What did you do?

We evaluated acebilustat in 199 adults from 18-30 years old with mild-to-moderate CF lung disease. People with any type of CFTR mutation were allowed to participate. The participants were randomly assigned to take acebilustat (50 mg), acebilustat (100 mg), or a placebo once daily by mouth for 48 weeks. The participants came to the study center for a research visit before they started their treatment, and then 10 times after treatment began, through the endo of the study. During the study, the participants continued to take all of their usual medications as they did before joining the study.

What did you find?

At the end of the study, researchers looked at lung function and pulmonary exacerbations in participants who got acebilustat in comparison to participants who got placebo. Overall, the results showed that lung function and pulmonary exacerbations were not any better in the participants who took acebilustat compared to participants without acebilustat. Participants who had higher lung function and/or who were using CFTR modulators tended to have the most improvement in exacerbation rates with acebilustat, but not enough to make definitive conclusions. Acebilustat was safe and well tolerated.

What does this mean and reasons for caution?

Acebilustat did not improve lung function or exacerbation rates sufficient to develop further at this time. As one of the larger studies of CF exacerbations in an era of CFTR modulator therapy, the results of this study gives researchers important information that will help them continue to develop drugs that can improve lung function and reduce pulmonary exacerbations in people with CF. Patients with mild disease may be more responsive to anti-inflammatory therapy, but sensitive tools will be needed to detect beneficial effects.

What's next?

While acebilustat was not efficacious for lung function improvements, the study taught important lessons about the target population, study subject selection, outcome measures, and clinical trial design that will need to be addressed to facilitated the development of anti-inflammatory therapy for people with CF.

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