



Cystic Fibrosis Research News

Title:

Efficacy and safety of ataluren in patients with nonsense-mutation cystic fibrosis not receiving chronic inhaled aminoglycosides: the international, randomized, double-blind, placebo-controlled Ataluren Confirmatory Trial in Cystic Fibrosis (ACT CF)

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What was your research question?

Does the drug ataluren reduce flare-up of lung infections (pulmonary exacerbations) and improve lung function in people with cystic fibrosis (CF) who have “nonsense” CFTR mutations and are not taking drugs called aminoglycosides, and is ataluren safe?

Why is this important?

CF results when the chloride channel protein (CFTR) made from the CFTR gene doesn't work well. Current CFTR modulators make CFTR protein work better, but nonsense mutations can't make any CFTR protein. For this reason, current modulators don't work well (or at all) on people with CF and nonsense mutations. Drugs like ataluren are called “read-through” agents and are believed to trick cells with nonsense mutations into making CFTR protein, but a recent study suggested that drugs called aminoglycosides might stop ataluren from working. If ataluren is safe and can help cells with nonsense mutations make CFTR protein when there are no aminoglycosides present, then it could be good treatment for people with CF and nonsense mutations.

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What did you do?

We conducted a clinical trial of ataluren in people with CF who had at least one nonsense CFTR mutation, were at least 6 years old with mild to moderate lung disease, and not treated with aminoglycosides. 279 volunteers from 75 sites in 16 countries received either ataluren or similar appearing placebo pills for 48 weeks. The change in lung function (by breathing tests) and number of pulmonary exacerbations requiring antibiotic treatment during the study were compared between people receiving ataluren and placebo.

What did you find?

People taking ataluren did not have better lung function than those not taking ataluren at the end of the study. Also, people taking ataluren didn't have fewer pulmonary exacerbations during the study. Ataluren appeared to be safe, but it didn't work as hoped.

What does this mean and reasons for caution?

Unfortunately, this means that ataluren will not be of benefit to people with nonsense-mutation CF. Further development of ataluren for treating CF has been halted.

What's next?

Other drugs that have the potential to be safe and effective for treating nonsense CFTR mutations are being studied in the laboratory in small groups of people with CF. Hopefully one of these drugs will reach the stage of being tested in people with CF and nonsense mutations.

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