



Cystic Fibrosis Research News

Title:

Inhaled mRNA Therapy for Treatment of Cystic Fibrosis: Interim Results of a Randomized, Double-blind, Placebo-Controlled Phase 1/2 Clinical Study

Lay Title:

Inhaled mRNA therapy for treatment of Cystic Fibrosis: Results of an Early Phase Clinical Trial

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What was your research question?

Can an inhaled formulation carrying a healthy form of the CF gene (CFTR messenger RNA (mRNA)) be safely delivered to people with CF?

Why is this important?

Treatment for people with CF has improved dramatically with medications such as triple combination modulator therapy that improves CFTR protein function. However, it is estimated that at least 10% of people with CF are either not candidates for this type of medication based on their genetics or do not experience benefit due to medication side effects. There is currently a need for new treatment approaches to fill this gap so that all people with CF can enjoy effective therapy. By delivering a normal copy of genetic instructions to airway cells, mRNA therapy could be effective for treatment of any type of CF mutation.

What did you do?

This was the first clinical trial of inhaled mRNA therapy in people with CF. Forty-two participants were enrolled in the study. In total 31 participants received at least one dose of mRNA therapy (MRT5005) and 11 received at least one dose of placebo. Four participants stopped treatment before receiving all of their doses, including 2 participants who had side effects (fever or allergic reaction) and 2 participants who stopped treatment due to COVID-related risks of continuing clinic visits for the study.

What did you find?

Common side effects in the month following study treatment included mild to moderate cough and headache. Ten participants experienced fever (and flu-like symptoms) about 4 -14 hours after treatment. These events were treated with medications (acetaminophen or ibuprofen) and cleared within 1-2 days. One participant had a pulmonary exacerbation requiring hospitalization approximately 3 weeks after receiving MRT5005. Two had symptoms consistent with an allergic reaction. They were treated with medications, and most symptoms were better by the next day. Lung function was repeatedly measured in each participant. No consistent patterns of increases or decreases in lung function were seen.

What does this mean and reasons for caution?

The results indicate that overall, MRT5005 was safe, but some participants experienced flu-like symptoms shortly after inhalation of this therapy. No consistent patterns of increases or decreases in lung function were seen, indicating that more work needs to be done before this



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approach to treatment can move forward in larger clinical trials. The authors are sincerely grateful to everyone who participated in the project, as future studies of new formulations of inhaled mRNA therapy for CF will benefit from the information learned from this trial.

What's next?

The next step is to develop more effective inhaled mRNA formulations. The goal will be to confirm in early (laboratory and animal) studies that these formulations can restore normal function of the CFTR protein in target airway cells with minimal inflammatory side effects.

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