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Cystic Fibrosis Research News

Title:

Answering the call to address cystic fibrosis treatment burden in the era of highly effective CFTR modulator therapy

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What was your research question?

We wondered how people with CF (PwCF), the families and acquaintances of PwCF, and clinicians who care for PwCF in the United States felt about the idea of studying the effects of withdrawing specific treatments now that highly effective CFTR modulators are available.

Why is this important?

It is important to study the effects of withdrawing specific treatments in PwCF taking highly effective CFTR modulators because we need to know if withdrawing those other treatments is safe. Although recent clinical trials of triple-combination CFTR modulators showed significant improvements in lung function and reduced risk of having a pulmonary exacerbation (a 'flare up' of lung disease), the PwCF who participated in these studies were also doing their chronic (long-term) treatments, included inhaled medications and airway clearance techniques. Because of the overlap of CFTR modulator and chronic treatments, the studies did not answer the question of whether it is safe to stop a chronic non-modulator treatment.

What did you do?

Using feedback from members of the lay, clinical, and research CF communities in the United States, we designed an electronic survey asking questions about withdrawing chronic treatments in PwCF who take a highly effective CFTR modulator. We used CF Foundation resources to distribute the survey widely. We asked PwCF if they had already stopped a non-

modulator treatment, how interested they were in participating in a treatment withdrawal trial, which treatments should be prioritized for this kind of trial, and what information was most useful as a sign of their overall health. The CF clinician survey contained similar questions.

What did you find?

We found that 80% (541/675) of CF community members and 94% (206/218) of CF clinicians thought that treatment withdrawal research should be done. We also found that 83% (299/359) of PwCF or community members speaking on behalf of a PwCF had not already stopped a chronic treatment. Community members ranked airway clearance techniques and inhaled antibiotics as the most burdensome chronic treatments. Clinicians were most interested in studying withdrawal of hypertonic saline and dornase alfa. Most community members and clinicians felt that a drop in lung function and/or increased daily symptoms were useful signs of a change in health status.

What does this mean and reasons for caution?

Our study confirmed that there is broad interest among stakeholders in the United States CF community for studying treatment withdrawal in the era of highly effective CFTR modulator treatment. The fact that most PwCF have not already stopped one or more chronic treatments means that we have a window of opportunity to perform this kind of research. We now know which chronic treatments are most worth studying in a withdrawal trial based on how burdensome they are to PwCF and/or family members. Change in lung function is a meaningful and easily measured endpoint in a trial of treatment withdrawal.

What's next?

The next step is to perform a clinical trial in the United States in which PwCF are randomly assigned to stop or continue using a chronic non-modulator treatment for a specified length of time. Change in percent-predicted forced expiratory volume in one second (ppFEV1) will be the primary outcome measure.

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