



Cystic Fibrosis Research News

Title:

Measuring the impact of CFTR modulation on sweat chloride in cystic fibrosis: Rationale and design of the CHEC-SC Study

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What was your research question?

The amount of chloride or salt in a person's sweat is used to diagnose CF. We wanted to know if sweat chloride values measured at CF diagnosis were similar to values measured at the time of starting a CFTR modulator/corrector, even if it has been many years after diagnosis.

Why is this important?

CFTR modulators change the amount of chloride in sweat. We wanted to know if the level of a person's sweat chloride changes when taking a modulator and if that predicts their future health. To do this, we need to measure the sweat chloride of thousands of people before and after starting modulators. If the amount of chloride in CF sweat is the same just before starting a modulator as when they were diagnosed, then we only need to measure their sweat chloride after they have started a modulator, which will make the study much simpler to run and more attractive to volunteers.

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What did you do?

We studied sweat chloride values of subjects who enrolled in two previous large CF studies. The GOAL study enrolled people with CF who were starting ivacaftor treatment and the PROSPECT study enrolled people with CF starting lumacaftor-ivacaftor treatment. We compared historic (diagnostic) sweat chloride values for subjects we got from the US CF Foundation registry with sweat chloride values measured before study subjects started taking modulators to see how similar they were. We also compared the change in sweat chloride after modulator treatment first to the individual's sweat chloride value just before starting modulator treatment and secondly to their historic (diagnostic) sweat chloride value.

What did you find?

We found that on average there was a very small difference between the historic sweat chloride values and the pre-modulator sweat chloride values, even when those measurements were separated by decades. Also, average changes in sweat chloride after taking modulators were the same when using historic values and when using values just before starting modulator treatment to calculate. We also found that sweat chloride values after starting modulator treatment measured after 1, 3, and 6 months of treatment stayed the same.

What does this mean and reasons for caution?

Our results mean that historic sweat chloride values obtained at CF diagnosis could be used in our study instead of measuring sweat chloride right before starting a modulator. This allowed us to design a study with only one research visit, after starting modulators, to measure sweat chloride values. One caution is that although average sweat chloride values were generally stable over time, large changes in sweat chloride were seen in some individuals. For this reason, it may be important to repeat sweat chloride measurements in certain individuals for clinical care.

What's next?

Our study, called CHEC-SC, is currently enrolling people with CF who have been prescribed modulators. We plan to enroll approximately 5,000 people and will study sweat chloride changes in different groups. We will also study how sweat chloride values predict future loss of lung function and rates of pulmonary exacerbations.

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