



Cystic Fibrosis Research News

Title: The Effects of Ivacaftor on CF Fatty Acid Metabolism: An Analysis from the GOAL Study

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What was your research question?

The drug ivacaftor has been shown to have clinical benefit for individuals with CF who have specific mutations, including G551D. However, there is much to learn about how ivacaftor works, including its effects on fatty acid metabolism (how fatty acids are processed for different functions in the body).

Individuals with CF have abnormalities in the metabolism of fatty acids, including omega-3 and omega-6 fatty acids (these are known as essential fatty acids), which may affect the course of CF disease by triggering inflammation (e.g. through the production of substances that promote inflammation called prostaglandins). Our research questioned whether ivacaftor improved fatty acid metabolism abnormalities or reduced production of prostaglandins.

Why is this important?

Essential fatty acid metabolism has an important role in inflammation that occurs in the body. In individuals with CF, abnormal fatty acid metabolism may play a role in the increased inflammation that leads to several features of CF disease. Understanding how ivacaftor may influence this process is important for understanding how best to use this drug and how to develop other drugs to help people with CF.

What did you do?

We utilized samples that were collected from 40 individuals with CF, who took part in a previous study referred to as the 'GOAL study'. In this study, participants were observed and blood and urine samples were collected before and after treatment with ivacaftor for six months. We used the samples to evaluate (1) fatty acid levels in the blood and (2) levels of an inflammatory prostaglandin product (called 'PGE-M'), that is produced from omega-6

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fatty acids and is measured in the urine. It can be used to indicate how much inflammation is present in the body (known as a 'marker of inflammation').

What did you find?

We found that ivacaftor did not change the fatty acid levels in the blood, but ivacaftor did decrease levels of PGE-M in the urine. In another study, PGE-M was shown to correlate with some signs of worse CF severity.

What does this mean and reasons for caution?

These observations may give further insight into how ivacaftor works. Many great clinical effects have been observed with ivacaftor and decreased PGE-M levels, found in our study, may reflect the decreased inflammation that is associated with some of the clinical improvements. However, as the fatty acid levels did not really change, this may indicate that ivacaftor does not fully correct every aspect of CF disease. These results need further investigation because this study included a relatively small group of individuals with CF and the observations reflect only 6 months of therapy with ivacaftor.

What's next?

These results need to be confirmed in a larger number of individuals with CF who have been taking ivacaftor for longer than 6 months. In addition, these interesting initial results present possible targets for future CF drug research.

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