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Cystic Fibrosis Research News

Title:

ALTERATIONS IN BLOOD LEUKOCYTES OF G551D-BEARING CYSTIC FIBROSIS PATIENTS UNDERGOING TREATMENT WITH IVACAFTOR

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What was your research question?

We attempted to answer the following question: “Does treatment with ivacaftor, a new drug used to treat some people with CF, change the activation of white blood cells?” Ivacaftor is used to treat patients with the G551D mutation in their CFTR gene and works by directly acting on the CFTR protein. This protein facilitates the movement of fluids and salts into and out of cells. In people with CF this protein does not function properly, and one side effect is the build-up of mucus in the lungs, which predisposes them to lung infections. Ivacaftor restores function in patients with the G551D mutation and reduces symptoms.

Why is this important?

Inflammation is a complicated process which the body uses to recognise, find and destroy foreign substances that are causing harm, such as bacteria.

White blood cells, specially a type called neutrophils, play a role in causing inflammation seen in the lungs of people with CF. This inflammation contributes to symptoms of the disease, especially when patients are experiencing a flare up in their lung infections.

What did you do?

Flow cytometry, is a specialised technique that uses lasers to identifying, categorise, sort and count cells within a fluid. We used flow cytometry in this experiment to identify changes in white blood cells from patients with and without the G551D mutation before and after treatment with ivacaftor.

We also took blood samples from 10 people with CF (individuals with the G551D mutation and also those with the delF508 mutation) and healthy people, and then we mixed this blood with ivacaftor to see if the drug had a direct effect on white blood cells.

What did you find?

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We know that white blood cells are activated when there is inflammation in the body. Before treatment with ivacaftor we found that the activity levels of the white blood cells were higher in people with CF than in people without CF. However, in the samples taken following treatment with ivacaftor the levels of white blood cells activity where similar in both groups.

What does this mean and reasons for caution?

These results suggest that ivacaftor is not just able to correct the CFTR function in the cells on the surface of the lungs, but may have additional effects. The results also offer an insight into the potential role of CFTR in how white blood cells function. There were only a few people providing data in these studies and, as a result, the findings should be viewed with caution. Furthermore, we could have looked at additional markers of white blood cell function to extend our findings on the impact of ivacaftor on activation.

What's next?

Additional studies will look at the impact of various combinations of agents to regulate CFTR on white blood cells and will use a broader range of measures to report on this. The result from these studies may show how, in future clinical trials, measuring people's immune function might indicate how they are responding to treatments with agents that regulate CFTR function.

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