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Cystic Fibrosis Research News

Title:
Idiopathic chronic pancreatitis treated with ivacaftor in a CFTR carrier with methylmalonic acidemia

Lay Title:
Treatment of Idiopathic Chronic Pancreatitis (ICP) with ivacaftor in a Cystic Fibrosis (CF) carrier who also had a second inherited risk factor for pancreatitis called Methylmalonic Acidemia

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What was your research question?
Can people with chronic pancreatitis, who are also carriers for cystic fibrosis (CF) due to a mutation in one copy of the *CFTR* gene, be helped by CFTR targeted drugs (like ivacaftor) that specifically improve the function of mutated CFTR proteins?

Why is this important?
Idiopathic chronic pancreatitis (ICP) is an extremely painful long term inflammation of the pancreas that can be debilitating and life-threatening. Patients with ICP often require recurrent hospitalizations or surgery and the use of chronic pain medications. There is currently no specific drug treatment for ICP. Carriers of CF are four times more likely than the general population to develop ICP. Medications (like ivacaftor) targeting CFTR dysfunction may be useful in the treatment of ICP in some people who are also CF carriers.

What did you do?
We report a patient who was hospitalized nine times in one year for ICP. She suffered from ethylmalonic acidemia (MMA), a rare metabolic disorder and known risk factor for ICP. She

was also found to be a carrier of a *CFTR* gene variant called R668C that was suspected to further increase her risk for ICP. Ivacaftor was previously shown to improve the function of the R668C variant in laboratory studies. Although ivacaftor is not approved for ICP treatment and the patient did not have CF, compassionate use of ivacaftor was approved to try to ease patient suffering as she was not a candidate for surgery.

What did you find?

The patient had a significant clinical improvement immediately after starting ivacaftor. First, her symptoms of pancreatitis resolved, and since commencing invacaftor she has not been hospitalized for ICP. Second, her pain medication usage reduced and was similar to her usage prior to her diagnosis of ICP. Third, repeat images of her pancreas showed a resolution of inflammation. Finally, levels of lipase in her blood, probably elevated due to pancreatic inflammation, significantly dropped, and were maintained within the normal range during ivacaftor therapy.

What does this mean and reasons for caution?

Chronic pancreatitis is thought to occur when there are multiple risk factors that lead to combined stress on the pancreas (such as MMA and being a CF carrier). This case study suggests that CFTR targeted therapies (like ivacaftor) may have a role in the treatment of ICP in CF carriers. Although a decrease in blood lipase levels and resolution of pancreatic inflammation on imaging after ivacaftor treatment are supportive of this, more patients need to be evaluated to definitively prove that ivacaftor is effective in treating IPC. Before commencing CFTR targeted therapies in people with ICP, it is important to determine if they are CF carriers and if they are, do they have CFTR variant that is predicted to respond to ivacaftor or similar medications.

What's next?

This report provides justification for future research studies of the treatment of ICP in CF carriers and to specifically determine if ivacaftor or other similar CFTR targeted therapies could be used reliably in this patient group.

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