Cystic Fibrosis Research News

Title:

Biliary disease and cholecystectomy after initiation of elexacaftor/ivacaftor/tezacaftor in adults with cystic fibrosis

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What was your research question?

Is elexacaftor/tezacaftor/ivacaftor (Trikafta), a new CFTR modulator combination therapy, associated with biliary and gallbladder complications shortly after initiation in certain high-risk patients?

Why is this important?

In trials, therapy with elexacaftor/tezacaftor/ivacaftor (Trikafta) has demonstrated to be highly effective and safe in people ≥ 12 years old with cystic fibrosis (CF) who carry at least one *F508del-CFTR mutation*. However, to date, no clinical trials or current literature have described biliary or gallbladder complications associated with starting CFTR modulator therapy. The most common biliary or gallbladder complications are biliary cirrhosis, gallstones, and gallbladder inflammation and are important to CF because they can lead to symptomatic disease that may require further management. This knowledge is needed for CF care team so that they can screen and educate patients for risk of these complications what signs or symptoms to look for.

What did you do?

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In this series of case summaries, we describe a potential, and previously unreported, side effect of gallbladder and biliary tract complications after the initiation of elexacaftor/tezacaftor/ivacaftor (Trikafta). We provide a brief summary of patients' medical history, the signs and symptoms they experienced that led to the diagnosis of this complication, and how they were treated. To further understand the patient cases we described, we reviewed the currently available information about how CF impacts the biliary tract and hypothesized how initiating elexacaftor/tezacaftor/ivacaftor (Trikafta) may further affect these organs.

What did you find?

Across our two adult CF care teams, we describe seven patients that experienced abdominal pain, nausea, and/or decreased appetite within 1 month after starting elexacaftor/tezacaftor/ivacaftor (Trikafta) and were later diagnosed with inflammation of their gallbladder or biliary tract. Six of these seven patients required surgery to have their gallbladder removed shortly after experiencing symptoms. All seven patients were able to remain on therapy with elexacaftor/tezacaftor/ivacaftor (Trikafta) after experiencing this complication.

What does this mean and reasons for caution?

Initiating elexacaftor/tezacaftor/ivacaftor (Trikafta) may increase the risk for gallbladder and biliary tract complications in certain patients. However, while we hypothesize that starting this medication led to these complications, without the controlled conditions of a clinical trial, we are unable to confirm the cause. The CF care team should be aware of this potential side effect and educate patients and staff to help identify patients efficiently. Patients experiencing severe abdominal pain, nausea, and/or decreased appetite shortly after starting therapy should inform their doctor for further evaluation.

What's next?

More information is needed to determine how starting elexacaftor/tezacaftor/ivacaftor (Trikafta) may impact the gallbladder and biliary tract of people with CF. The ongoing PROMISE study in the United States may shed some light on this and other effects of elexacaftor/tezacaftor/ivacaftor (Trikafta) outside of the lungs.

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