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Cystic Fibrosis Research News

Title:
Drug-Induced Liver Injury from Elexacaftor/Ivacaftor/Tezacaftor

Lay Title:
Drug-Induced Liver Injury from Elexacaftor/Ivacaftor/Tezacaftor

Authors:
Sarah Lowry[1]; Peter J. Mogayzel, Jr.[2]; Kiyoko Oshima[3]; Wikrom Karnsakul[1]

Affiliations:
[1]Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics,
[2]Eudowood Division of Pediatric Respiratory Sciences, Department of Pediatrics,
[3]Department of Pathology, Bloomberg School of Public Health, Johns Hopkins Medical Institutions, Baltimore, MD, USA

What was your research question? 50 words
We present a case report on drug-induced liver injury from Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEX/IVA) (Trikafta®, Kaftrio®).

Why is this important?
Cystic fibrosis (CF) is a life-shortening autosomal recessive disorder that is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene leading to abnormal ion transport. This leads to multiorgan dysfunction involving the lungs, pancreas, intestines and liver. A novel class of drugs known as CFTR modulators were developed to correct and improve the CFTR protein function and therefore organ function. A CFTR modulator combination medication, Elexacaftor/Tezacaftor/ Ivacaftor (ELX/TEZ/IVA) (Trikafta®, Kaftrio®), has been approved for patients older than age 6 since early 2020. Clinical trials have demonstrated significant improvement in physical symptoms and quality of life with ELX/TEZ/IVA.

What did you do?
We present a case report of a patient with CF who had a liver injury from ELX/TEZ/IVA.

What did you find?
We present a patient with CF with normal liver biochemistry and no known history of liver disease prior to initiation of therapy with ELX/TEZ/IVA. Five months after starting ELX/TEZ/IVA

laboratory testing demonstrated a mild transaminase elevation that worsened on repeat testing. Testing for infectious causes of transaminase elevation was negative. Due to worsening liver laboratory testing, liver biopsy was performed and demonstrated necrosis with moderate mixed lobular inflammation and mild portal inflammation without fibrosis or steatosis. Based on all combined history and testing results, drug-induced liver injury (DILI) was diagnosed. Transaminase levels returned to normal with the discontinuation of ELX/TEZ/IVA.

What does this mean and reasons for caution?

The use of CFTR modulators has changed the lives for many patients with cystic fibrosis. There have been previous reports of hepatic injury with patients taking CFTR modulators, however the long-term risk of hepatotoxicity is unknown. Understanding the impact of polypharmacy of medications for CF and drug metabolism are important to understand as patients with CF are living longer.

What's next?

Close monitoring of liver function with ELX/TEZ/IVA and possible dose adjustments if evidence of liver injury.

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