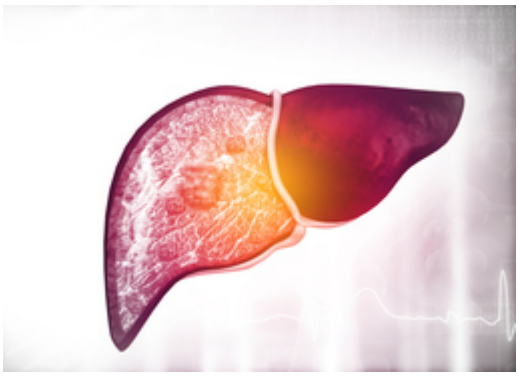
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

SGLT Inhibitor Drug for Treating Liver Diseases

TECHNOLOGY NUMBER: 2021-312



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Therapeutics and Vaccines
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OVERVIEW

Treatment of cystic fibrosis liver disease (CFLD) with a biologic inhibitor

- An agent that blocks sodium-glucose linked transporter (SGLT) receptors
- Improves liver function and decreases fibrosis in CFLD patients

BACKGROUND

Cystic fibrosis (CF) is a genetically transmitted disease with a prevalence of 1 in 3500 people living in North America. A mutation which alters transmembrane enzyme function and creates impaired movement of chloride ions across epithelial cell membranes, causing cell surface dehydration and the formation of a thick, sticky mucus. Patients most commonly suffer from lung dysfunction secondary to accumulation of this thick mucus in the airways, leading to lung infections and respiratory failure. However, CF is a multisystem disease which also impacts the epithelium of the pancreas, intestines, liver, and sweat glands.

Cystic fibrosis liver disease (CFLD) affects about 40% of CF patients and accounts for roughly one-third of CF-related deaths. CFLD may present with abnormal liver biochemistry levels, fat accumulation (hepatic steatosis), fat accumulation with inflammation (non-alcoholic steatohepatitis), cholestasis, fibrosis, and cirrhosis. These changes can eventually cause liver failure and death, more commonly in children but increasingly in patients who survive into their adulthood. The specifics of the pathogenesis of CFLD are poorly understood, and less research has been undertaken to address the effects of CF on the liver as compared to the lungs. Therefore, there is a significant need for the identification of novel therapies that specifically help CF patients diagnosed with CFLD to improve liver function, slow or stop progression of liver damage, prevent or delay liver transplantation, and increase overall survival.

INNOVATION

Researchers at the University of Michigan have discovered a means to treat CFLD by using an inhibitor originally approved for use in patients with diabetes mellitus. Sodium-glucose linked transporter (SGLT) receptors are responsible for glucose absorption in the intestines, kidneys, lungs, liver, and heart. SGLT inhibitors not only regulate glucose levels but also mediate help to mediate inflammation. The inventors of this technology provided animal data revealing that the use of the SGLT1/2 inhibitor Sotagliflozin can promote proper liver function, decrease inflammation, and increase long-term survival. These results are analogous to decreased inflammation, diminished fibrosis, and lower levels of fat accumulation in the livers of humans treated with SGLT inhibitors for obesity-associated non-alcoholic fatty liver disease (NAFLD). Therefore, SGLT inhibitors show promise toward aiding CFLD patients and diminishing the deleterious liver effects caused by CF.