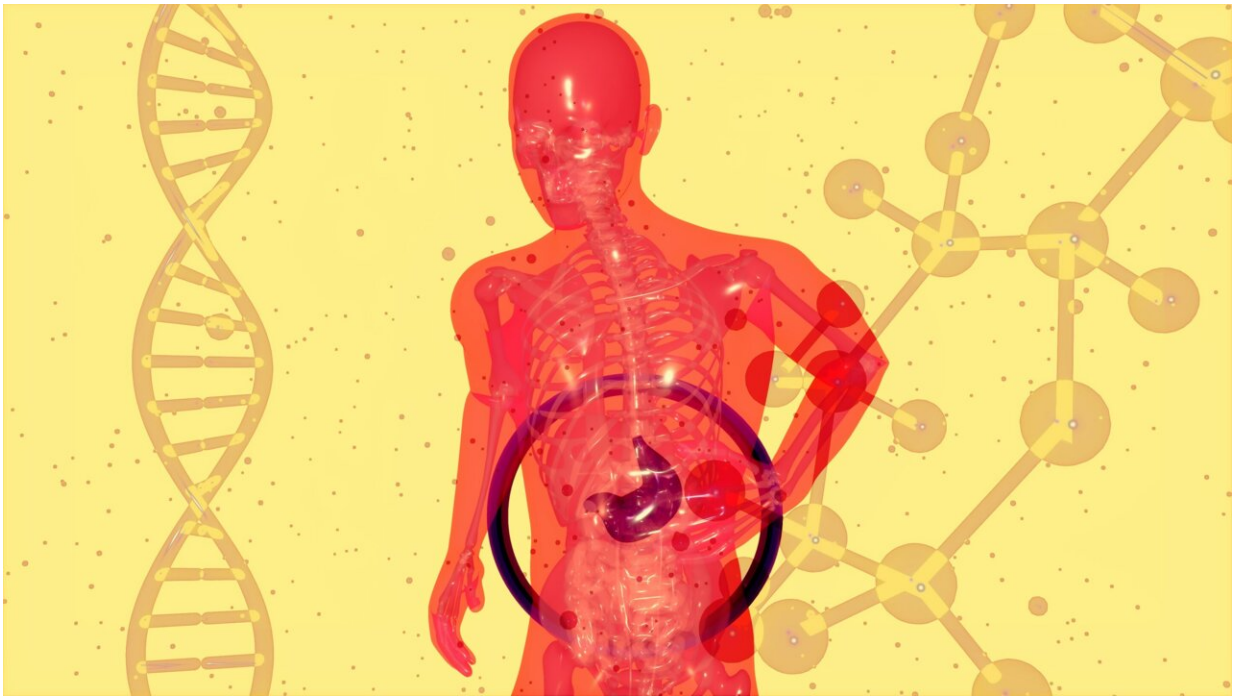
Experts help bring first-of-its-kind drug for metabolic liver disease to the clinic

March 15 2024



Credit: Unsplash/CC0 Public Domain

Liver disease specialists at the University of Chicago Medicine will soon begin prescribing a first-of-its-kind drug for treating advanced metabolic dysfunction-associated steatotic liver disease (MASLD)—formerly known as nonalcoholic fatty liver disease (NAFLD).

Resmetirom (to be sold under the brand name Rezdiffra), received FDA

approval on March 14, 2024. It is the first medication approved for treating metabolic dysfunction-associated steatohepatitis (MASH), a more advanced stage of MASLD characterized by liver inflammation and scarring known as fibrosis.

"Until now, liver disease has never had a treatment shown to reverse fibrosis, which is the damage from which all other issues stem," said Michael Charlton, MBBS, Director of the Transplant Institute at UChicago Medicine.

"If we can stop or slow fibrosis, we can theoretically prevent a lot of downstream consequences such as deaths, liver failure, liver cancer and the need for transplantation," said Mary Rinella, MD, Director of Metabolic and Fatty/Steatotic Liver Disease at UChicago Medicine.

Along with research colleagues from UChicago Medicine and other health institutions, Charlton and Rinella advised and contributed to a phase three clinical trial of resmetirom that reported positive results in February 2024. The paper is published in the *New England Journal of Medicine*.

"The study demonstrated—for the first time in a drug with a good side effect profile—improvement in fibrosis and less disease progression," Rinella said.

Since their metabolisms don't work properly, patients with MASLD usually have imbalances in the levels of lipids throughout their bodies, not just in their livers. As a result, there is a strong association between MASLD and cardiovascular complications like coronary heart disease and even heart failure.

In the recent trial, the researchers found that resmetirom not only improved fibrosis and inflammation in the liver for some patients but

also improved lipid levels for some patients.

"Between people whose disease progression halted and those who saw improvements in lipids and fibrosis, about two-thirds of patients had a favorable outcome with resmetirom," Charlton said. "We succeeded in something people didn't think could be done for this disease: we reached a biological endpoint." Biological endpoints are measurable health markers that regulators expect to be predictive of a treatment's clinical benefit.

Rinella, Charlton and their collaborators are continuing their research even as the drug enters the clinic, extending the phase three trial to examine long-term outcomes.

They pointed out that many people with MASLD don't know they have it because it is sometimes asymptomatic, especially if there is no fibrosis yet. Without symptoms, the disease only shows up on clinical tests like ultrasounds, blood tests or CT scans. Now that a drug exists that could reverse some liver damage and prevent future damage, they urged clinicians to work even harder to identify patients with MASH to maximize the impact of this breakthrough.

"We estimate that at least 25 million people in the United States could benefit from this drug, but only a small percentage of those have been identified in the clinic," Charlton said.

Once supplies become available for clinical use, specialists at UChicago Medicine will begin incorporating resmetirom into treatment plans for eligible patients as part of their comprehensive approach to metabolic liver disease treatment that also includes dietary therapy and lifestyle modification.

"One of the things that set UChicago Medicine's clinic apart is that we

have endocrinologists and dietitians embedded in our liver disease care teams to support patients through those changes they need to make," Rinella said.

More information: Stephen A. Harrison et al, A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2309000

Provided by University of Chicago Medical Center