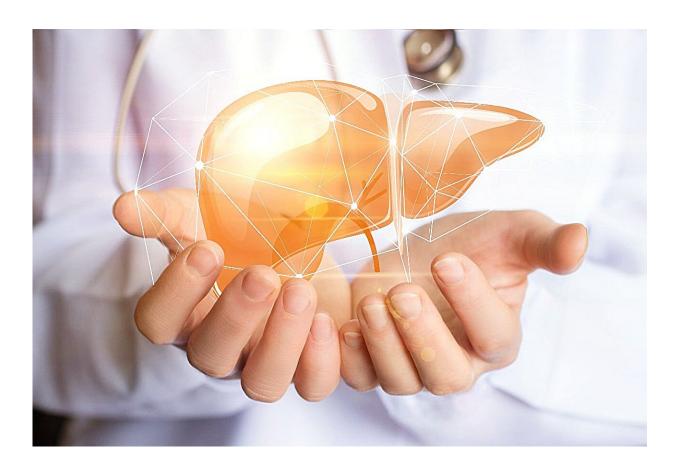


Experimental GLP-1 med may be breakthrough against fatty liver disease

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An experimental 'supercharged' form of popular GLP-1 weight-loss meds could help ease fatty liver disease, a new trial suggests.



The drug under development, survodutide, helped up to 83% of patients gain real improvements in markers of fatty liver disease, a widespread and potentially lethal condition often linked to obesity.

Right now, there's only one drug, resmetirom, approved by the U.S. Food and Drug Administration to fight fatty liver disease, and not all patients can use it.

Survodutide "could be a game-changer" against the illness, said study lead researcher Dr. Arun Sanyal. He directs the Stravitz-Sanyal Institute for Liver Disease and Metabolic Health and is a professor at Virginia Commonwealth University (VCU) in Richmond.

The trial was funded by Boehringer Ingelheim, the drug company developing survodutide. Results were published June 7 in the <u>New England Journal of Medicine</u>.

Fatty liver disease is shorthand for metabolic dysfunction-associated steatohepatitis (MASH). According to a news release from VCU, about 1 in every 4 people globally are affected by the condition.

A healthy liver has a fat content of just 5% or less by weight, but in MASH fat can rise to unhealthy levels that put people at risk for cirrhosis, <u>liver cancer</u> or even the need for a <u>liver transplant</u>. Obesity is a prime factor driving fatty liver disease.

The new trial isn't the first to suggest that a GLP-1 drug—a class that includes Ozempic, Wegovy, Mounjaro and Zepbound—might help ease MASH.

Another study, also led by Sanyal and funded by drugmaker Eli Lilly, found that its experimental GLP-1 drug, retatrutide, also helped reduce fat in the livers of obese people who took it. That study was presented



last November at the annual meeting of American Association for the Study of Liver Diseases in Boston.

The survodutide trial involved 282 adults from 25 countries, all of who had MASH with some level of fibrosis (scarring) of liver tissue. Patients received weekly injections of either a placebo or one of three doses of survodutide (2.4 milligrams, 4.8 mg or 6 mg) for 24 weeks.

The weekly dosage was gradually increased to 6 mg for another 24 weeks.

By the 48-week mark, most (83%) of patients saw improvements in a host of markers for fatty liver: lower levels of liver fat, inflammation and no worsening of fibrosis, Sanyal's team reported.

For three-quarters of the patients, their <u>fatty liver</u> disease had "resolved," meaning there was less fibrosis, inflammation and fat in the liver, and for 50% of the patients fibrosis and liver enzymes improved and there was no progression of their disease.

In common with other GLP-1 meds, gastrointestinal side effects did occur, such as nausea, diarrhea and vomiting, the researchers noted.

As explained by Sanyal, survodutide is a "dual agonist" drug, meaning that it contains two agonists—hormone mimics—that bind with brain receptors to help with weight loss.

While standard GLP-1 meds like Ozempic contain one agonist mimicking the hormone glucagon-like peptide 1 (GLP-1), survodutide contains a GLP-1 agonist plus an agonist against glucagon, a hormone that helps control blood sugar.

From mouse studies, his team believed that a dual-agonist drug might



better target fat in the liver, improving on the effect of standard GLP-1 medicines.

The new trial seems to have confirmed that in people.

"These data demonstrate that direct liver targeting with glucagon agonism in addition to GLP-1 effects helps resolves nonalcoholic <u>fatty liver disease</u> and improve fibrosis while maintaining the benefits of GLP-1 agonism," Sanyal said in a university news release.

"These findings are remarkable and exciting and open a new chapter in drug development for MASH with fibrosis, where a single agent could potentially target both the liver disease and related medical conditions may provide hope for millions who have both MASH with fibrosis and multiple obesity-related ailments," Sanyal said.

More information: Find out more about fatty liver disease or MASH at the <u>Cleveland Clinic</u>.

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