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Phase 2 trial finds obesity drugs lower fibrosis markers in alcohol-related liver disease

In 270 patients, five active regimens beat placebo on noninvasive measures, but the study did not test clinical outcomes

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Drugs first developed for metabolic liver disease and obesity showed early signs that they may reduce liver fibrosis markers in people with alcohol-related liver disease, according to phase 2 trial results presented at The Liver Meeting 2026 in Denver.

The study enrolled 270 participants with heavy alcohol use and advanced liver disease and randomly assigned them to 28 weeks of once-weekly treatment with zalfermin, cagrilintide, semaglutide, or one of two drug combinations, or to placebo. Investigators reported that every active treatment group met the trial’s primary endpoint by lowering Enhanced Liver Fibrosis, or ELF, scores compared with placebo. They also reported consistent improvements in liver stiffness and in PRO-C3, another noninvasive marker linked to fibrosis.

Vijay Shah, a consultant in the Division of Gastroenterology and Hepatology at Mayo Clinic in Rochester, Minnesota, discussed the findings in an interview with HCP Live. He said the trial was based in part on the biological overlap between alcohol-related liver disease and metabolic dysfunction-associated steatotic liver disease, including its inflammatory form, MASH. In practical terms, he said, liver tissue from a patient with MASH and liver tissue from a patient with alcohol-related disease can look very similar under the microscope.

That overlap led researchers to test therapies aimed at pathways already under study in MASH and obesity. Zalfermin is an FGF-21 analog, cagrilintide is an amylin analog, and semaglutide, sold for obesity under the brand name Wegovy, is a GLP-1 receptor agonist.

Investigators described the study as the first randomized trial to show that a drug treatment can improve fibrosis biomarkers in alcohol-related liver disease. That is a notable step in a field where treatment options remain limited. Current clinical guidance says sustained abstinence is still the cornerstone of care for alcohol-associated liver disease, and there are no approved drugs that directly target the underlying fibrogenic process.

The results, however, remain preliminary. The trial measured changes in noninvasive biomarkers rather than hard clinical outcomes such as liver failure, hospitalization, transplant, or survival. The findings also do not mean heavy drinking is safe while taking these drugs.

One key question was whether any apparent liver benefit simply reflected less alcohol use. According to Shah, alcohol consumption trended down in every study group, including placebo, but the differences between active treatment and placebo were not statistically significant. That pattern suggests the improvement in fibrosis markers may have come at least partly from direct effects on the liver, rather than from a clear reduction in drinking caused by the medications.

Shah also said many participants appeared to have metabolic risk factors consistent with what researchers call the MetALD phenotype, a mixed pattern in which alcohol-related liver injury coexists with metabolic dysfunction. That may help explain why drugs being developed for MASH could also show activity in alcohol-related disease.

The findings could add to a broader health debate that matters to the beverage industry, because they advance research into liver damage associated with alcohol use while also underlining that the central medical advice remains unchanged: reducing or stopping alcohol consumption is still essential. The trial did not show that the drugs reduced drinking compared with placebo, and it did not weaken the link between heavy alcohol use and serious liver harm.

The data were presented in an abstract by Shah and colleagues during the November 5-9 liver meeting in Denver. Researchers said future studies will need to address the safety and tolerability of these therapies in people who continue to drink heavily, as well as the challenge of designing trials in a population where alcohol use patterns can shift over time. They also said any eventual role for these medicines would most likely be alongside treatment for alcohol use disorder, not as a replacement for it.