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**Glucagon-like peptide-1 receptor agonists and risk of major adverse liver outcomes in patients with chronic liver disease and type 2 diabetes**

*Wester A, Shang Y, Grip E,*et al*.*[*Glucagon-like peptide-1 receptor agonists and risk of major adverse liver outcomes in patients with chronic liver disease and type 2 diabetes.*](https://gut.bmj.com/content/73/5/835)Gut *2024; 73: 835–843. doi: 10.1136/gutjnl-2023-330962.*

It has been suggested in Phase II trials glucagon-like peptide-1 receptor (GLP1) agonists might resolve metabolic dysfunction associated steatohepatitis. The effect of these medications on the effect of clinical outcomes in patients with chronic liver diseases (CLD) of any aetiology and concurrent type 2 diabetes is still unknown.

Wester et al., conducted a target trial emulation of observation data using Swedish healthcare registers to evaluate the long-term casual effect of GLP1 agonists on the risk of major adverse liver outcomes (MALO) such as decompensated cirrhosis, hepatocellular cancer (HCC), liver transplantation or MALO-related death in patients with CLD and type 2 diabetes. An inverse-probability weighted structural model was used to compare the 10-year MALO risk between GLP-1 agonist initiators and non-initiators. Observational analogs of the intention-to-treat (ITT) and per-protocol effects were estimated. In the per-protocol analysis, patients were censored if they deviated from their assigned treatment strategy.

The study included 1026 GLP-1 agonist initiators and 15633 non-initiators. According to the ITT analysis, the 10-year risk of MALO was 13.3% in initiators compared to 14.6% in non-initiators (risk ratio (RR) = 0.91, 95% CI = 0.50-1.32). The corresponding 10-year per-protocol risk estimates were 7.4% and 14.4%, respectively (RR = 0.51, 95% CI = 0.14-0.88).

The results of this study suggest that GLP1 agonists may result in lower risk of MALO in patients with CLD and type 2 diabetes who initiated and adhered to GLP1 therapy over time. The use of target trial emulation approach allowed Wester et al., to investigate the long-term causal effect of GLP 1 agonists on the risk of MALO using large national healthcare registers, while randomized controlled trials using MALO as an outcome might be unfeasible. This study supports the potential role of GLP1 agonists in reducing risk of CLD progression in patients with concurrent type 2 diabetes.