

## Oral GLP-1 Receptor Agonists Can Reduce Heart Failure

Heart failure is a common complication in patients with type 2 diabetes. In the double-blind, placebo-controlled, randomized, multicenter phase 3b clinical trial SOUL (Semaglutide Cardiovascular Outcomes Trial), oral semaglutides reduced the risk of major adverse cardiovascular events, consisting of cardiovascular death, nonfatal myocardial infarction, or non fatal stroke, in patients with type 2 diabetes. Whether oral semaglutides also affect the severity of heart failure was the subject of a secondary analysis of the SOUL study.

The study participants (n = 9650), with a median age of 66 years, had type 2 diabetes and atherosclerotic cardiovascular disease and/or chronic kidney disease. They were stratified according to the presence (23.1%) or absence of heart failure at the start of the study. Among participants with heart failure, 10.3% had heart failure with preserved ejection fraction (HFpEF), 6.1% had heart failure with reduced ejection fraction, and 6.7% had an unknown subtype.

Study participants were randomly assigned to receive either oral semaglutide or placebo once daily in addition to their standard treatment, which could include SGLT2 inhibitors and mineralocorticoid receptor antagonists. The prespecified composite heart failure outcome of interest consisted of heart failure-related hospitalization, heart failure-related emergency treatment, or cardiovascular death after a median follow-up of approximately four years (47.5 months).

The analysis showed that the risk of reaching the combined heart failure endpoint was reduced by 22% in patients with preexisting heart failure receiving oral semaglutides compared to the placebo group (hazard ratio [HR]: 0.78; 95% confidence interval [CI]: 0.63–0.96), especially in patients with HFpEF. However, in patients without a history of heart failure the risk did not change (HR: 1.01; 95% CI: 0.84–1.20). The frequency of serious adverse events in participants with heart failure was similar between oral semaglutide (53.8%) and placebo (57.1%).

The authors conclude that this data indicates a potential additional benefit from oral semaglutide in reducing heart failure-related events in patients with type 2 diabetes and heart failure.

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Source: Pop-Busui R et al.: Oral Semaglutide and Heart Failure Outcomes in Persons With Type 2 Diabetes: A Secondary Analysis of the SOUL Randomised Clinical Trial. *JAMA Intern Med.* Published online 2 February 2026. doi:10.1001/jamainternmed.2025.777