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DIABETES

Cardiovascular benefits of semaglutide

Semaglutide, a glucagon-like peptide 1 analogue, reduces the rate of cardiovascular events in patients with type 2 diabetes mellitus who are at high cardiovascular risk. These findings from the SUSTAIN-6 trial were published in *The New England Journal of Medicine*.

Of the 3,297 patients included in the trial, 83% had established cardiovascular disease, chronic kidney disease, or both. Patients were receiving a standard-care regimen, and were randomly assigned to receive once-weekly semaglutide (0.5 mg or 1.0 mg) or placebo for 104 weeks.

The primary outcome (first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) occurred in 6.6% and 8.9% of the semaglutide and placebo groups, respectively (HR 0.74, 95% CI 0.58–0.95, $P<0.001$ for noninferiority). This result was driven by a significant reduction in nonfatal stroke in the semaglutide group (1.6% vs 2.7%; HR 0.61, 95% CI 0.38–0.99, $P=0.04$), and a nonsignificant trend towards a reduction in nonfatal myocardial infarction (2.9% vs 3.9%; HR 0.74, 95% CI 0.51–1.08, $P=0.12$); the rate of cardiovascular death was similar in the two groups (2.7% vs 2.8%). Clinically meaningful reductions in glycated haemoglobin level, body mass, and systolic blood pressure might have contributed to the lowering of cardiovascular risk with semaglutide.

Semaglutide therapy was associated with lower rates of new or worsening nephropathy, but a significantly increased rate of retinopathy complications (HR 1.76, 95% CI 1.11–2.78, $P=0.02$). Serious adverse events occurred less frequently in the semaglutide group, but more patients discontinued treatment because of adverse events, mainly gastrointestinal.

The reduction in cardiovascular events associated with semaglutide is consistent with trials showing improved cardiovascular outcomes with liraglutide (another glucagon-like peptide 1 inhibitor) and empagliflozin (a sodium–glucose cotransporter 2 inhibitor).

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