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# Effects of exenatide on cardiovascular outcomes in patients with type 2 diabetes mellitus: results of the EXSCEL study

Objective:

The once weekly weekly GLP-1 receptor agonist depot exenatide is approved for lowering the blood glucose level in type 2 diabetes (T2D). Depot exenatide also leads to reductions in body weight, blood pressure and lipid levels. To investigate the effects of depot exenatide in addition to standard diabetes care on cardiovascular outcomes in T2D patients, the EXSCEL study was conducted.

Methodology:

In the double-blind, placebo-controlled, pragmatic study, T2D patients with or without cardiovascular disease were randomized to 2 mg depot exenatide or placebo. The primary endpoint was defined as the time to first occurrence of the composite 3-point MACE endpoint (cardiovascular death, non-fatal stroke, non-fatal myocardial infarction).

Results:

A total of 14,752 patients with a median observation period of 3.2 years were included in the intention-to-treat population. In 10,782 (73.1%), there was a cardiovascular disease. The mean exposure duration was 2.4 years with depot exenatide and 2.3 years with placebo. The primary endpoint occurred in 839 out of 7,356 patients in the exenatide group (11.4%, 3.7 events per 100 patient years) and 905 out of 7,396 patients in the placebo group (12.2%, 4.0 events per year) 100 patient years) (HR 0.91 [95% CI: 0.83; 1.00]). In terms of the safety hypothesis, the intention-to-treat analysis demonstrated non-inferiority of depot exenatide versus placebo ($p < 0.001$); no efficacy could be demonstrated in terms of efficacy hypothesis ($p = 0.06$). Overall mortality was significantly reduced as a secondary endpoint ($p < 0.016$). Confirmed cases of acute pancreatitis were rare overall and were similar in both treatment groups. The rates of serious adverse events did not differ.

Conclusion:

The EXSCEL study did not show significant differences in the incidence of major cardiovascular events among depot exenatide versus placebo in T2D patients with and without cardiovascular disease.