Abstract: **5257**

Effects of once-weekly exenatide on clinical outcomes in the subgroup of patients with pre-existing cardiovascular disease: insights from EXSCEL

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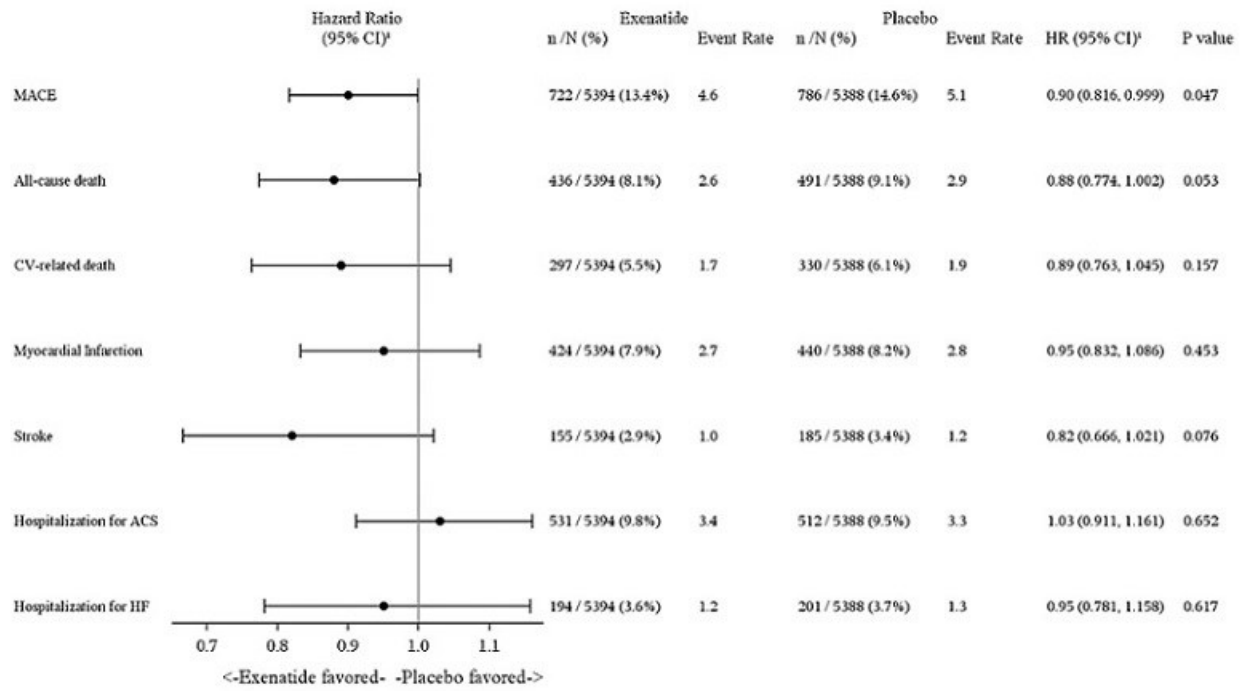
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Background: EXSCEL showed a non-significant reduction in major adverse cardiovascular events (MACE) and a nominally significant reduction in all-cause mortality when once-weekly exenatide was added to usual care for type 2 diabetes. A pre-specified subgroup analysis of treatment effects for the primary endpoint of MACE and other EXSCEL cardiovascular (CV) outcomes was performed in patients with known CV disease at baseline.

Methods: We evaluated outcomes by treatment group in the EXSCEL trial for the 10,782 participants (73% of the trial population) with known CV disease, i.e. history of major clinical manifestation of coronary artery disease, ischemic cerebrovascular disease or atherosclerotic peripheral arterial disease. Cox proportional hazards were used to compare the impact of once-weekly exenatide with placebo therapy on MACE, all-cause death, CV-related death, myocardial infarction, stroke, hospitalization for acute coronary syndrome (hACS) and hospitalization for heart failure.

Results: Patients in the exenatide group demonstrated a 10% relative risk reduction for MACE (HR, 0.90, 95% confidence interval 0.816 to 0.999, nominal p-value 0.047). Each of the secondary endpoints favored exenatide, compared with placebo, with the exception of hACS [Hazard Ratio (HR), 1.03], but none met the nominal level of statistical significance (all nominal P>0.05) (Figure).

Conclusion: Exenatide once-weekly reduced the risk of MACE in a subgroup of patients with pre-existing CV disease in EXSCEL with no new or overall safety concerns.

Figure. Forest plot of Clinical Endpoints in the Intent to Treat Population with a Known History of Cardiovascular Disease at Baseline. Abbreviations: MACE indicates major adverse cardiac events; CV, cardiovascular; ACS, acute coronary syndrome; HF, heart failure; CI, confidence interval; HR, hazard ratio.

	Hazard Ratio (95% CI)[1]	Exenatide n /N (%)	Event Rate	Placebo n /N (%)	Event Rate	HR (95% CI)[1]	P value
MACE		722 / 5394 (13.4%)	4.6	786 / 5388 (14.6%)	5.1	0.90 (0.816, 0.999)	0.047
All-cause death		436 / 5394 (8.1%)	2.6	491 / 5388 (9.1%)	2.9	0.88 (0.774, 1.002)	0.053
CV-related death		297 / 5394 (5.5%)	1.7	330 / 5388 (6.1%)	1.9	0.89 (0.763, 1.045)	0.157
Myocardial Infarction		424 / 5394 (7.9%)	2.7	440 / 5388 (8.2%)	2.8	0.95 (0.832, 1.086)	0.453
Stroke		155 / 5394 (2.9%)	1.0	185 / 5388 (3.4%)	1.2	0.82 (0.666, 1.021)	0.076
Hospitalization for ACS		531 / 5394 (9.8%)	3.4	512 / 5388 (9.5%)	3.3	1.03 (0.911, 1.161)	0.652
Hospitalization for HF		194 / 5394 (3.6%)	1.2	201 / 5388 (3.7%)	1.3	0.95 (0.781, 1.158)	0.617

0.7 0.8 0.9 1.0 1.1

<-Exenatide favored- -Placebo favored->

[1]Hazard ratio (active/placebo) and CI are based on Cox proportional hazards regression model with treatment group only as explanatory variable.