Effect of Exenatide Once-Weekly on Clinical Outcomes in Patients With Type 2 Diabetes Mellitus and Cardiovascular Disease: Insights From the EXSCEL Trial

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Background: Several cardiovascular (CV) outcomes trials of antihyperglycemic agents in patients with type 2 diabetes mellitus (T2DM) have demonstrated reductions in major adverse CV events (MACE) including mortality. EXSCEL topline results demonstrated that exenatide once-weekly did not increase CV risk based on the composite measure of MACE and showed a consistent safety profile among patients with and without CV disease. Fewer CV events were observed in the exenatide arm; however, the efficacy objective of reduction in CV risk did not reach statistical significance. The full results on the effect of exenatide once-weekly in patients with CV disease and the associated profile of response are pending.

Methods/Results: EXSCEL was an international, randomized, placebo-controlled pragmatic trial of the GLP-1 receptor agonist exenatide once-weekly in 14,752 patients with T2DM and a wide range of CV risk (i.e., with and without a prior CV event at baseline). Approximately 70% (N=10,782) of patients had at least one prior CV event (70% CAD, 24% PAD; 22% CVA). Analyses are underway to evaluate clinical outcomes and treatment responses specifically in patients with a prior CV event. Analytic methods will include risk modeling using Cox proportional hazards models and analysis of the relationship between baseline clinical factors, randomized treatment and clinical outcomes. Key predictors will be identified using a backward variable selection process and bootstrapping methods.

Conclusions: Following the presentation of the primary EXSCEL results at the EASD on September 14, 2017, the present analysis will represent the first key secondary analysis from the largest GLP-1 receptor agonist trial completed to date. Results from the presentation will focus on the group of patients with baseline CV disease and factors associated with all-cause mortality and CV outcomes.