New TECOS analysis adds heart failure data for Sitagliptin

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Patients with type-2 diabetes and cardiovascular disease can safely take the antihyperglycemic drug sitagliptin without an increased risk of cardiovascular complications - even if they have a history of heart failure - a new analysis of the TECOS (Trial Evaluating Cardiovascular Outcomes with Sitagliptin) study shows.

The findings, presented today at ESC Congress 2015, "provide reassurance to patients and prescribers about the cardiovascular safety of sitagliptin" - a dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin – according to Paul Armstrong, MD, one of the investigators of the study, from the University of Alberta in Edmonton, Canada.

The initial TECOS findings, presented earlier this year at the American Diabetes Association, were adjusted to control for baseline heart failure, which, "although this was a pre-specified endpoint, left some questions unanswered," explained the Darren McGuire, MD, first author of the study, from University of Texas Southwestern Medical Center, in Dallas, Texas, USA.

"Now we present unadjusted analyses (also pre-specified) with identical results, and we complement these with mulitivariable analyses - all yielding the identical conclusion: no signal of any sort for heart failure risk with sitagliptin," said Dr. McGuire.

"The stability of these findings across a very extensive set of complementary/sensitivity analyses is completely reassuring, both scientifically and for patients and providers, that no matter how we sliced and diced the data the same result was observed," he said.

Previous studies (SAVOR-TIMI 53 and EXAMINE) have associated DPP-4 inhibitors with increased risk of heart failure, making the TECOS findings "very important, not only for endocrinologists, but also for cardiologists who see many patients with diabetes and coronary heart disease treated with sitagliptin," noted Dr. Armstrong.

"Because heart failure has been associated with some treatments for diabetes, it's comforting to know that sitagliptin can be used safely without that concern."

The study involved 14,671 patients with type-2 diabetes and established cardiovascular disease, who were randomized to receive sitagliptin (n=7,332) or placebo (n=7,339) added to usual care, with the addition of other antihyperglycemic medications when necessary in both groups to achieve glycemic control.

In previously reported findings, after a median follow-up of 2.9 years, sitagliptin met the primary endpoint of non-inferiority compared to placebo for the composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke or hospitalisation for unstable angina.

Additionally hospitalisation for heart failure was no different between the two groups after adjustment for baseline heart failure status (HR 1.00; 95% CI 0.83-1.20).

Now, new unadjusted results and mulitivariable analyses show a similar picture (HR 1.00; 95% CI 0.84-1.20; and HR 1.02; 95% CI 0.83-1.26).

"Through extensive complementary analyses, we observed the same reassuring signal of heart failure safety of sitagliptin when analysing all heart failure events (first and recurrent); when analysing heart failure in composite analyses with CV and all-cause death; and across extensive subgroup analyses of 22 factors-importantly including presence or absence of heart failure at baseline," said Dr. McGuire.

"Adding these data to those from SAVOR TIMI-53 and EXAMINE with regard to hospitalization for

heart failure, the two key observations are that there is a moderate degree of heterogeneity between the results from each of these trials of DPP4 inhibitors; and that, when pooled in meta-analysis, the incremental risk for heart failure is no longer statistically significant (HR 1.14; 95% CI 0.97-1.34)," he concluded.

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