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Impact of sitagliptin on cardiovascular and safety-related outcomes in insulin-treated type 2 diabetes: the TECOS experience

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Background and aims: The Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) was a randomized, double-blind, placebo-controlled trial that assessed the cardiovascular (CV) safety of sitagliptin when added to existing glucose-lowering therapies in 14,671 patients with type 2 diabetes and prior CV disease. The large subset of patients treated with insulin at baseline (N=3,408) provides an opportunity to examine the impact on glycaemic, cardiovascular, and safety-related outcomes when sitagliptin is added to insulin therapy.
Materials and methods: Baseline demographic, diabetes-related and cardiovascular characteristics were summarized for patients on insulin compared with other glucose-lowering therapies. Among insulin-treated patients, HbA_{1c} and estimated GFR (eGFR) changes over time, and rates of key cardiovascular endpoints, severe hypoglycaemic episodes and diabetes-related complications were examined in the intent-to-treat population for sitagliptin vs. placebo-treated patients. Serious adverse events (SAEs) were also examined in the randomized population that received ≥1 dose of study medication.
Results: Those treated with insulin at baseline, compared with non-insulin-treated patients, were slightly older (66.1 vs. 65.3 years), had longer diabetes duration (17.1 vs. 9.9 years), higher HbA_{1c} (7.4% vs. 7.2%), lower eGFR (71.0 vs. 76.1 ml/min/1.73m²), and were more likely to have prior heart failure (22.6% vs. 16.6%). A lower HbA_{1c} was seen at 4 months in patients using insulin at baseline allocated to sitagliptin (0.39%) compared with placebo, and over the study duration (0.30%, $p<0.001$ for both). Similar rates were observed for severe hypoglycemia (3.5% vs. 4.0%), a composite of major adverse cardiovascular events (12.4% vs. 12.3%), the individual components of the composite [CV-related death (4.4% vs. 4.6%), nonfatal MI (5.5% vs. 5.7%) and nonfatal stroke (2.4% vs. 2.0%)], and hospitalizations for heart failure (3.9% vs. 4.8%) in the sitagliptin and placebo groups respectively. Rates of diabetes-related complications and SAEs were also similar in the two treatment groups (Table).
Conclusion: In TECOS, among patients treated with insulin at baseline, similar rates of cardiovascular outcomes, diabetes-related complications and SAEs were observed in the sitagliptin and placebo treatment groups. The slightly greater reduction in HbA_{1c} seen with the addition of sitagliptin did not result in an increase in the incidence of severe hypoglycemia.

Proportion of Insulin-treated Patients with Incident Complications of:	Insulin + Sitagliptin (N=1,724)	Insulin + Placebo (N=1,684)
Serious Adverse Events	14.3%	13.1%
Diabetic eye disease	5.6%	4.2%
Diabetic nephropathy	8.7%	9.0%
Renal failure	1.8%	2.3%
Diabetic neuropathy	5.4%	5.0%
Peripheral arterial disease	3.8%	3.3%
Amputation	1.5%	1.9%
Gangrene	1.0%	1.4%

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