

## Sitagliptin and Risk of Heart Failure in Patients With Type 2 Diabetes

### A Meta-Analysis

We are interested in the editorial comment by Margulies (1) in which he suggested that the glucagon-like polypeptide (GLP)-1 improves glycemic control by increasing insulin sensitivity in both skeletal muscle and adipose tissue. Sitagliptin, a dipeptidyl peptidase (DPP)-4 inhibitor, suppresses glucagon hormone and increases endogenous insulin by increasing GLP-1 level. However, to date, many studies have presented conflicting results regarding the safety of sitagliptin on heart failure (HF). Thus, we performed a systematic review and meta-analysis of all studies to determine the strength of the relationship between sitagliptin use and the incidence of HF in patients with type 2 diabetes mellitus (T2DM).

We conducted a comprehensive search of MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Scopus, and the Cochrane Central Register of Controlled Trials from database inception through April 3, 2016. Studies were included if they reported the associations between sitagliptin use and the incidence of HF in patients with T2DM. Using the DerSimonian and Laird random effects models, we calculated pooled risk ratios with 95% confidence intervals. Heterogeneity was assessed by using the Cochran Q test and the  $I^2$  statistic.

From retrieved articles, 10 studies with a total of 340,747 diabetic patients with 11,419 total HF events were included for this meta-analysis. The pooled analysis demonstrated that sitagliptin exposure was not associated with the incidence of HF (risk ratio: 0.98; 95% confidence interval: 0.83 to 1.16;  $p = 0.84$ ,



$I^2 = 65.5\%$ ;  $P_{\text{heterogeneity}} = 0.002$ ). The possible mechanisms underlying the association of sitagliptin with HF remain controversial. Although some studies (2-4) found that sitagliptin use was associated with an increased risk of HF, there were potential confounders that needed to be adjusted, such as general T2DM medication (thiazolidinediones), severity of HF, and type of HF (systolic vs. diastolic).

In conclusion, we did not find that sitagliptin use was associated with increased risk of HF in patients with T2DM. However, current evidence might not be sufficient to draw the final conclusion and therefore further studies are still needed to make an assertion.

\*Chayakrit Krittanawong, MD

Takeshi Kitai, MD, PhD

Mehmet Aydar, PhD

Tao Sun, MD, PhD

\*Department of Cardiovascular Medicine

Heart and Vascular Institute

Cleveland Clinic

9500 Euclid Avenue

Desk J3-4 (WT)

Cleveland, Ohio 44195

E-mail: [Krittac@ccf.org](mailto:Krittac@ccf.org)

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