

Format for ANSWERING REVIEWERS

July 12, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (ESPS Manuscript NO: 13480).

Title: Incretins and selective renal sodium-glucose co-transporter 2 inhibitors in hypertension and coronary heart disease

Author: Ramiro A Sanchez, Hugo Sanabria, Cecilia de los Santos, Agustin J Ramirez

Name of Journal: *World Journal of Diabetes*

ESPS Manuscript NO: 13480

The manuscript has been improved according to the suggestions of reviewers and We highlighted the changes made to the manuscript according to the peer-reviewers' comments as requested;

Thank you for your evaluation.

1) Lenguistic errors were corrected and a general idiomatic task was added.

2) Abbreviations were explained in the text

3) Conclusions were re designed and sentence other studies with was omitted

CONCLUSION

These new anti-diabetic compounds have shown additive CV protective effects in T2DM. Additional benefits include lowering of blood pressure, improvement of lipid profile and endothelial dysfunction, decrease in the macrophage-mediated inflammatory response, and reduction of myocardial injury. All these effects were mainly evaluated in animal models, since human clinical studies that include a high number of participants are still missing.

On the other hand, there are ongoing studies that aim to evaluate the CV effect and the safety of DPP-IV inhibitors. From the last studies that were published in which DPP-IV inhibitors were used, SAVOR TIMI, TECOS and EXAMINE, it seems that a neutral cardiovascular effect rather than a benefit is expected for these compounds. There are other studies with DPP-IV, which are still being developed, such as CAROLINA and CARMELINA, so additional effects could still be assessed.

As it was previously mentioned, further investigations in large cohorts of diabetic patients are needed in order to assess the exact mechanisms of CV protective effects held by renal glucose transport inhibitors. The reason supporting this need is based on the fact that these compounds have shown interesting natriuretic effect resulting in blood pressure decrease and loss of weight. Further trials may endorse these clinical features

Thank you

Ramiro Sanchez,MD,PhD, FAHA