

Format for ANSWERING REVIEWERS

March 21, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 16507-Review.doc).

Title: Interpretation of cardiovascular outcome trials in type 2 diabetes needs a multiaxial approach

Author: Odd Erik Johansen

Name of Journal: *World Journal of Diabetes*

ESPS Manuscript NO: 16507

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

(1) Response to reviewer 1:

In its invited editorial manuscript, Dr. Johansen quickly reviews the main completed and ongoing clinical trials aiming at improving glycaemic control and diminishing CV burden in T2D. Importantly, this editorial addresses the issue of how results should be interpreted, taking into account the fact that the primary outcome of a study might not be fully informative, and not reproduced between independent studies. The reasons for this are quickly surveyed, and include intrinsic differences among studies such as the duration of the disease at the time of recruitment, the duration of the intervention and the different therapeutic approaches investigated (DPP4 inhibitors, GLP1R analogues, SGLT2 inhibitors). The editorial is interesting and informative, and the two well-designed figures are informative of the future developments we may expect based on ongoing major clinical trials. I have just a few concerns relative to this manuscript, mainly editorial in nature. Page 2, line 15 : replace ? works ? with ? work ?. Page 3 line 13 : typo : ? apparently ? ; line 16 : replace ? was ? with ? were ? ; Page 4, line 7 from bottom : Perhaps rephrase as : ? This was illustrated, for example, by the PROactive.... ?Page 5 : replace CVOT with ? cardiovascular outcome trials ? , CVOT was not defined before in the text. References : for consistency, remove D.O.I. from references 7, 9. For reference 21, mention ? in press ?.

Response:

Thank you for your comments. In the revised manuscript I have revisions in line with the suggestions of the reviewer and the changes are highlighted below:

Page 2, line 15 : replace ? works ? with ? work ?.

Typo has been revised (now stating "work")

Page 3 line 13 : typo : ? apparently ? ;

Revised to correct spelling (now stating “apparently”)

line 16 : replace ? was ? with ? were ?

Revised “was” to “were”.

Page 4, line 7 from bottom : Perhaps rephrase as : ? This was illustrated, for example, by the PROactive.... ?

Revised as per reviewer suggestion.

Page 5 : replace CVOT with ? cardiovascular outcome trials ? , CVOT was not defined before in the text.

“CVOTs” has been replaced with “CV outcome trials”

References : for consistency, remove D.O.I. from references 7, 9. For reference 21, mention ? in press ?

As per editorial office request, all references have now been revised to include PubMed citation numbers and DOI citation coder. Further, all references now list all authors.

(2) Response to reviewer 2:

The editorial proposed with the title: "Cardiovascular outcome trials in type 2 diabetes in the context of disease burden and degree of vasculopathy: the need for a multidimensional approach to result interpretation" is a good analysis and criticism of the difference studies about cardiovascular disease in type 2 diabetes mellitus where the author studies the different trials and the future of them in the next years, and is an opportunity for great learnings. Some studies contribute to our approach to type 2 diabetes mellitus but in the future they need to taking into account the disease duration, degree of vasculopathy, duration of the intervention, and the mode of action of the intervention. With this fully support an optimized patient centered approach to type 2 diabetes mellitus and the cardiovascular risk will be reached.

Response:

Thank you for these overall comments to the paper.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Diabetes*.

Sincere regards,

Odd Erik Johansen, MD, PhD