Author’s response to reviews

Title: Short-term effectiveness of low dose liraglutide in combination with metformin versus high dose liraglutide alone in treatment of obese PCOS: randomized trial

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Author’s response to reviews:

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Ref. Short-term effectiveness of low dose liraglutide in combination with metformin versus high dose liraglutide alone in treatment of obese PCOS: randomized trial (BEND-D-16-00195)
Mojca Jensterle1, Nika Aleksandra Kravos1, Katja Goričar2, Andrej Janez1
Dear Professor Michael O'Reilly,

We would like to sincerely thank you and to the Reviewers for the revision of our manuscript and for providing valuable remarks and suggestions. We have fully revised the manuscript in the light of yours and the Reviewer’s comments and hope you will now find the revised version suitable for publication in your journal.

The revised article is attached.

We look forward to hearing from you.

Sincerely yours,

Mojca Jensterle
Andrej Janez

Answers to the Reviewers’ comments:

Reviewer 1

Identified no issues to address.

Reviewer 2

Q1. As this is aimed at women with PCOS, it will be important to address the effect it may cause in case the patient might become pregnant whilst on the treatment. Hence, I would advice a section of safety profile on GLP-1 analogues in pregnancy and may be a disclaimer explaining the same to the patient.

A1: We addressed the suggested issue in the Methods section, page 6, lines 140-144. We added a reference No. 24 that has been recently reported about normal pregnancy outcome after first-trimester exposure to liraglutide in women with type 2 diabetes. We believe that the Reviewer 2 raised a very important point not just because of the limited knowledge regarding safety issue but also because some recent animal studies suggested that GLP-1 may play a major role in reproduction according to the animal studies discussed in the article reported on http://www.medpagetoday.com/endocrinology/infertility/53094
Q2: Although the paper includes an extensive pre- and post- comparison in the two groups, it is necessary to show that both groups did not have any significant difference between them before conclusions could be drawn about one treatment being superior than the other.

A2: As recommended by the reviewer, we included data on comparison of pretreatment values between both groups. There were no statistically significant differences between both groups. We included all the necessary changes in the manuscript:

• information on the statistical analysis: Methods section, Statistical analysis, line 153-154, page 7 (“To compare the pretreatment values and the change of clinical parameters among different treatment groups, nonparametric Mann-Whitney test was used.”)

• results of the analysis: Results section, Baseline results, lines 165-166, page 7 (“There were no statistically significant differences between both groups (Table 1).”); and Table 1 (column “Comparison of pretreatment values between groups”).