

We thank the Reviewers and the Editors for their time and effort spent on our work titled “Progesterone in gender-affirming therapy of trans women” which was submitted to the *World Journal of Biological Chemistry* [Manuscript NO: 74322]. Please see below for our responses to comments from the Reviewers and the Editors of the Journal.

Reviewer # 1 [05720477]:

Although the manuscript does not add essentially anything new to what is already known, presenting it as a minireview is, in fact, correct, and this may still be of interest to the readers of the World Journal of Biochemistry. I don't think I have any particular advice as the work is well conducted, structured and written.

We Thank the Reviewer for the kind comments.

Reviewer # 2 [05244179]:

The article doesn't bring clarity for the role of Progesterone in gender-affirming therapy of trans women, as the title suggests. Description of progesterone role in trans women needs detailing, at present more focus is on progesterone role in general. The conclusion should specify the article's contribution towards existing literature with recent references.

We thank the Reviewer for his/her opinion and advice. It is true that the role of progesterone in gender-affirming treatment is currently vague. There are no reliable studies (actually there are almost no studies at all) on this specific issue so far. Therefore, the potential benefits from the addition of progesterone on top of oestradiol in the therapy of trans women can only be theoretically presumed. Our article has elaborated on the physiologic properties of progesterone because these can form the basis for future investigation of the administration of progesterone in transgender females. Nonetheless, the conclusion section has been expanded in order to specify the article’s contribution to the existing literature and guide the formation of future research questions, as Reviewer #2 suggests.

Comments from the Journal’s Science Editor:

This manuscript explored the potential clinical implications of adding bioidentical progesterone to gender-affirming therapy in transgender women. It is recommended to elaborate on the role of progesterone in transgender women, enrich the citations of references

in the conclusion, and specify the contribution of the article to the existing literature as well as recent references.

We thank the Journal's Science Editor for the valuable suggestions. We would like to underline that the role of progesterone in gender transition cannot be currently based on research evidence because of the lack of relevant studies. Our article points out that only hypotheses can be formed from the extrapolation of data existing from studies among cisgender women. As the Journal's Science Editor suggests, the conclusion section has been expanded in order to elaborate on the hypothetical role of progesterone in gender affirming therapy of trans women. The provided references in the additional text indicate the current status of the existing literature on this issue.

Comments from the Company's Editor-in-chief:

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden.

We thank the Editor-In-Chief for the reminder. The table has been reformatted in the revised version of the manuscript