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To:

World Journal of Gastroenterology

Piraeus, September 2022

Dear Editor-in-Chief,

We would like to thank you for the thoughtful evaluation of our review article entitled “**The interplay between metabolic dysfunction-associated fatty liver disease and chronic kidney disease; Epidemiology, pathophysiologic mechanisms, and treatment considerations**” and for the most welcome comments that helped us to improve the presentation of our article. We read the comments carefully and we tried to address them all; thus, we are now pleased to submit the revised version of the manuscript for consideration by the World Journal of Gastroenterology.

Below we provide a point-by-point response to all comments in a separate rebuttal letter. Specifically, please find listed below our point-by point response (in normal font) to the comments (in bold). Moreover, our revised Text is adjusted to all the requirements, as per journal style and according to the editor-in-chief’s remarks.

A potential publication of our work in your journal would be great honor for our study group.

We thank you for your time and consideration on our behalf.

Sincerely yours,

Dr. Panagiotis Theofilis

Reviewer #1:

I would like to commend the authors for very well written article on highly relevant topic. In my opinion the manuscript should be accepted for publication following the minor revision that will address these points: - Starting from section “Therapeutic approaches” citing literature is incorrect - The existing clinical data on tirzepatide should be mentioned (e.g. Diabetes Care 2020;43:1352-1355) - The text requires slight technical, grammar, and language polishing - The list of references should be revised in order to make it uniform in style

Reply: We thank the reviewer for the time and effort spent on the assessment of our manuscript and we are please with his/her overall impression.

Regarding the mentioned incorrectly cited literature starting from the section “Therapeutic approaches”, we state that Table 1 contains several references (69 through 90), which are responsible for the gap within the main text. We went ahead to reevaluate the reference list in this specific part of the manuscript and found no mistakes.

Tirzepatide is a promising therapeutic option in cardiometabolic diseases and we apologize for not mentioning latest study results concerning hepatic steatosis and NASH. The relevant studies are now being mentioned in the main text (references 109-110).

*Please see the revised “**Glucagon-like peptide 1 receptor agonists**” section:*

“Concerning clinical evidence, tirzepatide dose-dependently ameliorated biomarkers of NASH such as alanine transaminase, aspartate aminotransferase, keratin-18, and procollagen III compared to placebo. At the same time, it was associated with an increase in adiponectin^[109]. Lastly, in a recently published substudy of the SURPASS-3 MRI clinical trial, administration of tirzepatide in patients with T2DM decreased the liver fat content along

with the volume of visceral and abdominal subcutaneous adipose tissue, compared to insulin degludec^[110].”

Finally, we proceeded to another English check to correct any further mistakes present while the reference list was reevaluated to add any missing information on page/article number or PMID.

Reviewer #2:

The topic selection of this manuscript is very novel, focusing on the association between newly proposed MAFLD and CKD, and comprehensively reviewing the flow disease, pathophysiology, treatment and other aspects. Especially in terms of treatment, it gives clinicians a very good perspective.

Reply: We are excited with the reviewer’s opinion regarding our manuscript and we thank him/her for assessing it thoroughly.