

Dear editor and referee,

Thank you for your consideration of and comments on our manuscript (59633-Meta-Analysis) entitled " **Novel glucose-lowering drugs for non-alcoholic fatty liver disease: a systematic review and meta-analysis of randomized controlled trials**". Attached please find the revised manuscript. Our responses to the reviewer's comments are as follows:

- 1、 In the Abstract, the authors state that the difference between GLP-1RAs and SGLT2 inhibitors in ALT change was significant in favour of GLP-1RAs, but in the Results section they say the difference was not significant – please reconcile this inconsistency.

Response: Thank you for your suggestion. We have revised the abstract.

- 2、 The limitations of the available data need further discussion. While ALT and AST changes were the primary outcome measure, these are only really indirect endpoints. A more important endpoint is differences in the rate of progression of fibrosis or the emergence of cirrhosis. Similarly, all the trials are relatively short in duration compared to the timescale of progression of NAFLD; this represents a major limitation. It would be interesting to see some analysis of how closely the changes in ALT or liver fat are related to the loss in body weight associated with these drug classes – ie. are the benefits for NAFLD in proportion, or out of proportion, to their propensity to induce weight loss?

Response: We admit that the histological progression or resolution is recognized as the "gold standard" of disease evaluation. However, after literature search, only few controlled trials with histological outcome were found. In this context, we used the indirect measures—changes in ALT and AST levels, as the primary outcome measures. We added the discussion about these limitations. In the revised

manuscript, we added the meta-regression analyses about association between the changes in transaminase, body fat composition and weight loss.

- 3、 The authors talk about a “decrease in ALT change” in the Abstract and the Results section. What they mean is a “decrease in ALT”. Similarly, although the manuscript is accompanied by an English Editing Certificate, there are a number of errors of English expression, particularly in the area of singulars vs plurals and in the use of the definite and indefinite article. There also seems to be a typo where we are told that “two independent investigators (XXX and XXX) conducted systematic searches”.

Response: We edited the language and corrected the typo in the revised manuscript.

We thank the reviewer again for their valuable comments. We hope that our responses are satisfactory, and we look forward to hearing from you.

Best regards.

Sincerely yours,

Yufeng Li