Dear Reviewer of World Journal of Hepatology,

Subject: Response to Reviewer's Comments on Manuscript ID 89459

I hope this letter finds you well. I would like to express my gratitude for your thorough review of our manuscript entitled Associations of *PNPLA3* and *LEP* genetic polymorphisms with metabolic associated fatty liver disease in Thai people living with HIV. Your insightful comments have greatly contributed to the enhancement of the scientific rigor and clarity of our work.

I appreciate the specific feedback you provided, and I have addressed each of your concerns as follows:

1. Description of the ART Treatment:

I have carefully revised the section describing the antiretroviral therapy (ART) treatment, incorporating additional clarification on the impact of nucleoside reverse transcriptase inhibitors (NRTIs) and protease inhibitors (PIs) on hepatocyte cell death and mitochondrial dysfunction. I have also expanded on the references provided to strengthen the scientific foundation of our statements.

The nucleoside reverse transcriptase inhibitors (NRTIs) within the Antiretroviral Therapy (ART) regimen, including zidovudine, stavudine, and didanosine, have the potential to induce hepatocyte cell death through the mitochondrial-induced apoptosis pathway [1-4]. Conversely, the more recent generation of NRTIs, such as tenofovir, abacavir, lamivudine, and emtricitabine, exhibits minimal impact on mitochondrial dysfunction and does not significantly contribute to the development of Metabolic Associated Fatty Liver Disease (MAFLD through this specific mechanism [5-6].

Additionally, the effects of Protease Inhibitors (PIs) used in HIV treatment on metabolism exhibit variability. Early-generation PIs, such as indinavir and ritonavir, can induce insulin resistance and have negative metabolic effects. In contrast, other PIs, like atazanavir and darunavir, demonstrate a more favorable profile in terms of insulin resistance [7-8]. In conclusion, individuals with HIV are more susceptible to developing MAFLD due to the direct effects of the virus. Nevertheless, it appears that the newer antiretroviral medications have a reduced detrimental impact on the development of MAFLD in these individuals. However, our study did not identify ART regimen NRTI-based and PI-based as predictive factors for Metabolic Associated Fatty Liver Disease (MAFLD).

Please review the revised manuscript, and I trust that these modifications have addressed your concerns regarding the description of the ART treatment.

References

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2. Platelets Count and Hemoglobin Levels:

I have revisited the results section and re-emphasized the analysis of platelet count and hemoglobin levels, which are now presented in Table 1. The statistical comparison between people living with HIV (PLWH) with MAFLD and those without MAFLD has been clearly stated. The findings indicate that there was no statistically significant difference in platelet count between these two groups.

I hope these additional details adequately address your query about platelet count and hemoglobin levels.

3. Rewriting the Discussion Section:

I have taken your feedback into consideration and have extensively revised the discussion section, placing a particular emphasis on the role of ART treatment in the

development of MAFLD. The revised manuscript has undergone professional English language editing to ensure clarity and coherence in presenting our arguments.

I trust that these changes have substantially improved the quality of the discussion section, and I invite you to review the updated manuscript.

Once again, thank you for your valuable feedback and the time you dedicated to reviewing our manuscript. I believe that the revisions made have strengthened the overall quality of our work. I look forward to receiving your feedback on the updated manuscript.

Thank you for your consideration.

Sincerely Yours,

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