May 9, 2020

Editor-in-Chief
World Journal of Hepatology

RE: MS ID 55718 entitled " Real-world safety and effectiveness of sofosbuvir and ribavirin for elderly patients over 75 years old"

Dear Editor-in-Chief

Thank you very much for your letter dated April 27, 2020. We found the comments from the referees very constructive. After taking the reviewers' comments into account, we made substantial revisions and would now like to resubmit our manuscript for publication. The details of the changes are summarized below.

We hope that you will find the changes satisfactory. Thank you again in advance for your kind consideration of our work.

Sincerely,

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Below are our responses to the reviewer's comments (MS ID 55718)

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: It is good study. A study to support the drug use of elderly patients. The number of patients could be higher. it would be better if there were more patients

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Regarding the manuscript entitled "Real-world safety and effectiveness of sofosbuvir and ribavirin for elderly patients over 75 years old", the authors evaluated the safety and efficacy of Sofosbuvir plus ribavirin in old age patients and they concluded that this combination is safe and effective in the treatment of HCV infection in elder patients. This manuscript is of interest but contains many problems that required substantial modification:

1- The title is not confirmed with the manuscript methodology. It should be rewritten.

→ Based on this comment, we have corrected the title for the manuscript.

2- The aim of the study is not clear and need to be related to the methodology used.

→ Following the advice from the reviewer, the purpose of this study has been rewritten (page 3, lines 5-7; page 6, lines 3-5).

3- Sample size calculation is missed.

→ As requested, we have explained how the study size was determined (page 6, line 24-24).

4- The introduction section only one side effect of ribavirin, I recommended to mention the other side effect as well as the side effect of sofosbuvir.

→ In accordance with this comment, we have mentioned other side effects of ribavirin and have added a comment regarding side effects of sofosbuvir (page 5, lines 19-21).

5- Also, introduction section required more references to provide the accurate information.

→ As advised, we have added more references to substantiate our comments.

6- Organization of results section is not accurate, please rewrite again.

→ The Results section has been reorganized, as requested.

7- There are some English errors; I recommended grammar and typos errors revisions.

→ Based on this comment, we have had the manuscript re-checked by a native speaker.

8- Figure legends should contain full explanatory data, please complete it

→ Following this advice, we have added full explanatory data to the figure legends.

Reviewer #3:
Scientific Quality: Grade C (Good)
Language Quality: Grade C (A great deal of language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: This study evaluated the safety and efficacy of Sofosbuvir plus ribavirin especially for elderly patients in a real-world setting. Title: The authors used the term "elderly patients over 75 Years". The authors included patients above and below 75 Years (range 17-86). Thus, this titled is misleading and showed that the authors included only patients over 75 Years.

→ As suggested, we have corrected the title of the study.

Abstract: The study aim is also focused on the elderly patients over 75 years. It should be modified to include the comparison of patients above and below 75 years. The order of reporting the results is not accurate. The authors started by the patient's discontinuation and ended by the SVR. The authors should reorder the information by reporting the SVR results then the safety results.

→ As advised, the purpose of this study has been rewritten (page 3, lines 5-7; page 6, lines 3-5), and the order of reporting results has been amended.

Introduction: -It should be consistent and directly related to the topic in good writing flow. More than 60% of the reported data related to the ribavirin dose reduction, which was not the main core of this study. They did not report any information related to the study treatment regimen (sofosbuvir plus ribavirin) -Only 3 references in the introduction means lack of information page 5, line 9: please report the other side effects of ribavirin

→ Following this advice from the reviewer, we have added more references to the Introduction section (page 5, lines 2-9). We have also mentioned other side effects of ribavirin and have added a comment regarding side effects of sofosbuvir (page 5, lines 19-21).

Methods: - No sample size calculation and justification was provided - the anthers conducted this study Between June 2015 and June 2017, why they did not include the results of long-term follow-up instead on only SVR12. Reporting the results of relapse or re infection is important. - Study flow diagram of included patients should be provided as per the STROBE checklist to determine the number of screened patients, patients completed the study, patients discontinued, patient's response. - logistic regression analysis might be effective to determine the most important factors for SVR. - study endpoint should be determined clearly in the methods - definition of the treatment failure should be included.

→ Based on these comments, we have explained how the study size was determined (page 6, line 22-24). As the SVR24 rate was equivalent to the SVR12 rate, we have redefined SVR as SVR24 in the revised text. Patient flow was explained in the Results section (page 9, lines 6-9). Following the advice from the reviewer, logistic regression analysis was performed to investigate the most important factors for SVR (Table 3). Definitions of treatment response, study endpoint and treatment failure have been clarified in the revised text (page 8, lines 3-8).

Results: - The most important baseline chch should be reported in the rest of the results section. - Treatment effectiveness should be reported before the safety. - Treatment response section should be written again to be for clear.

→ As suggested, we have provided important baseline characteristics (page 9, lines 9-15). Treatment effectiveness has been reported before safety. The treatment response section has been rewritten for clarity.

Discussion: Clear and comprehensive General: the overall manuscript is good but it needs careful medical writing revision.

→ Based on this comment from the reviewer, the manuscript has been re-checked by a native speaker.

(1) *Science Editor*: Although the comments are good, the CrossCheck detection showed a high similarity to published articles (total 33%), which is not eligible. Recommendation: Rejection.

(2) *Editorial Office Director*: I have checked the comments written by the science editor. Based on the peer-review report, I suggest a potential acceptance with minor revision. The language of the manuscript should be polished. As I checked, the highest single-source similarity index (18%) was caused by the "materials and methods" section, which showed a high similarity compared with the authors' previous published article.

(3) *Company Editor-in-Chief*: I have reviewed the Peer-Review Report and the full text of the manuscript, of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revision. In addition, we strongly suggest our authors to adhere to the spirit of ethical writing and avoid reusing their own previously published text.

→Based on these comments, the manuscript has been re-checked by a native speaker, and we have added some sentences into "materials and methods" section to be clearly understood.