

July 2, 2022

Dear Editors-in-Chief

Peter Schemmer, FACS, MD, Ph.D., Chairman, Professor

Re: Submission of a re-revised manuscript to the WORLD JOURNAL OF GASTROINTESTINAL SURGERY

Thank you very much for giving us the opportunity to revise our *invited review* (Manuscript NO: 75503)

We would be grateful for the consideration of our revised manuscript "*Sirolimus versus tacrolimus: which one is the best therapeutic option for patients undergoing liver transplantation for hepatocellular carcinoma?*" (by Faiza Ahmed, Faiza Zakaria, Godsgift Enebong Nya, and Mohamad Awf Mouchli) for publication in the *World Journal of Gastrointestinal Surgery*.

The authors have read and complied with author guidelines, and they all have seen and approved this manuscript for publication. None of the authors had a conflict of interest to disclose concerning this manuscript.

We are grateful to the Editors for their precious contributions and comments. We hope that you will now find it suitable for publication in the *World Journal of Gastrointestinal Surgery*. In case of final acceptance, we agree to make this manuscript open-access.

Below you can find a point-by-point reply to the reviewers.

Thank you for your precious time.

We are looking forward to receiving your decision in due time.

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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Any specific groups of patients Change from tacrolimus to mTor The authors Ahmad F et al have reviewed literature of Sirolimus versus tacrolimus: which one is the best therapeutic option for patients undergoing liver transplantation for hepatocellular carcinoma? The letter to the editor is in response to an article by Zhao et al . Trends of rapamycin in survival benefits of liver transplantation for hepatocellular carcinoma. World J Gastrointest Surg 2021; 13: 953-966 who have detailed mechanistic advantages of mTOR inhibitors in HCC and suggested advantages of this treatment with immuno therapy to prevent recurrences. mTOR inhibitors like Rapamycin and Everolimus have anti proliferative actions and have been shown to improve survival in liver transplantation in patients with hepatocellular carcinoma in some studies, though there are other studies with no advantages. The authors have reviewed the current literature extensively however in the conclusion leave the readers with something wanting more than a simple conclusion that more studies are needed to understand safety profile of mTOR inhibitors in comparison to tacrolimus. It might help the readers more if they could comment if there is evidence that some specific subgroup of patients will be better of on mTOR inhibitors than tacrolimus amongst the whole group – e.g. patients with or without acute kidney injury or renal dysfunction as tacrolimus is potentially nephrotoxic, however mTOR inhibitors might delay recovery of renal tubular necrosis. It may be that this group of patients need to be included in the future studies of liver transplants for patients with hepato cellular carcinoma. Overall the review is good and provides a balanced evaluation of current literature.

Thank you for taking some time out of your busy schedule to review our manuscript. My main aim with this letter was to provide direct comparative studies of the two drugs, but unfortunately, I found very less information published in the electronic search databases. Since sirolimus is much more recent than tacrolimus in the field of liver transplantation, there is limited data available from hospital settings. I believe what you are looking for can be written extensively within a literature review as a

letter is not sufficient to describe these two drugs' potential. Whatever data I found within my search I did my best to include it in the letter. Moreover, my aim was to write on recent data (year limit 2020-2021), not on papers that were already published in the past. As there are other manuscripts (literature reviews, systematic reviews, meta-analysis) which have written separately on these two drugs prior to year 2020, but none has done any direct comparison. I submitted this manuscript to the journal on January 31, 2022. Since I was invited to write a letter for the journal, I took a month to work on this letter with my team (as we take our time to make sure the manuscript is perfected prior to submission), and we stopped our database search at year limit December 2021. Hence, whatever data I found within my search limit, I have done my best to include it in the letter.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Authors summarized the recent literature published missing at Zhao Yat al.'s paper on survival benefit of sirolimus in patients with liver transplantation for HCC. I strongly suggest to add a summary table to this Letter to the Editor.

Thank you for taking some time out of your busy schedule to review our manuscript. I kindly decline your suggestion, as we do not want to lengthen the letter. A letter is supposed to be short and to the point for the readers, as that is how I like to read letters published in journals. We do not wish to include a summary table, as the data written is sufficient in its available format.

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Thank you for taking some time out of your busy schedule to review our manuscript. We are extremely happy to see your positive comments.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Surgery, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Thank you for taking some time out of your busy schedule to review our manuscript. Dear Editor, we submitted this letter on January 31, 2022 to your prestigious journal. Our search limit was set from January 2020 to December 2021. Our aim was to bring out recent publications on these two drugs and write a letter (because other publications such as narrative review, systematic review, meta-analysis, and letters did not include articles starting from the year 2020). Since we required one month to write, edit, and perfect the letter, we could only search up to December 2021. And once done, we submitted the letter to you on January 31, 2022. I checked the RCA link and found a few articles published after my submission to your journal. I also checked PubMed and found 82 recent publications for tacrolimus and 24 recent publications for sirolimus for liver transplantation. I cannot go through these recent publications and rewrite the letter as these manuscripts were published after my submission. I had submitted two letters simultaneously to your journal and one of them is already in article in press, and this one is pending. I kindly request you to understand my situation, as I cannot redo the search to update new data in the letter.