Dear Editor-in-Chief,

RE: Manuscript number 67781

Thank you for the careful review and insightful comments on our manuscript entitled "Gastrointestinal and hepatic side effects of potential treatment for COVID-19 and vaccination in patients with chronic liver diseases". We have revised the manuscript in response to these comments. Please find below an explanation of how these comments have been addressed.

Reviewer #1:

Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision

Specific Comments to Authors: The submitted article is valuable as regard it try to discuss the GIT and hepatic side effects of drugs and vaccines used for treatment of COVID-19 patients with chronic liver diseases, but some comments to be considered:

1 - it is better to enlist drugs used in COVID-19 according to the life cycle of the virus to detect potential targets for drug therapy (Promising drug targets include nonstructural proteins (eg, 3-chymotrypsin-like protease, papain- like protease, RNA-dependent RNA polymerase), which share homology with other novel coronaviruses (nCoVs). Additional drug targets include viral entry and immune regulation pathways.)

> Response: Thank you for this suggestion. The discussion on these drugs is now structured according to where they act in the life cycle of the virus, and a new figure has been added (Figure 1) to illustrate this point.

2 - many drugs were not listed or discussed

i - Umifenovir (Arbidol)which inhibit S protein/ACE2,membrane fusion inhibitor(200 mg every8h by mouth 7-14 d. Available as: 50-mg and 100-mg tablets, capsules and granules. Dose adjustments: Kidney: no dose adjustment necessary. Hepatic: No specific recommendations available, caution in those with hepatic impairment.

Response: A section on umifenovir has been added to the manuscript on page 6.

ii - Favipiravir: RNA polymerase inhibitor Exclusion criteria based Hyperuricemia, diarrhea, elevated transaminases.

Response: A section on favipiravir has been added to the manuscript on page 14-15.

iii - Nitazoxanide, traditionally an antihelminthic agent, has broad antiviral activity and a relatively favorable safety profile. Nitazoxanide has demonstrated in vitro antiviral activity against MERS and SARS-CoV-2. Pending further evidence, the antiviral activity, immunomodulatory effects, and safety profile of nitazoxanide warrant its further study as a treatment option for SARS-CoV-2.

Response: A section on nitazoxanide has been added to the manuscript on page 16-17.iv - Ivermectin: Ivermectin is thought to block the cargo transporter which means the virus can't get into the nucleus, and so can't make copies of itself. Avery interesting clinical trial using combinations of theses drugs not cited(Hatem Elalfy , Effect of a combination of Nitazoxanide, Ribavirin and Ivermectin plus zinc supplement (MANS.NRIZ study) on the clearance of mild COVID-19. J Med Virol. 2021 :1-8 doi: 10.1002/jmv.26880. Online ahead of print. PMID: 33590901.

Response: A section on ivermectin has been added to the manuscript on page 16-17, and the suggested reference has been cited in the manuscript.

v - Molnupiravir is an antiviral drug that is in clinical trials aiming to treat coronavirus. It's been said that it has shown some use against other viruses such as

SARS and MERS. Its been designed to treat deaths and hospitalizations, but it also prevents transmission.

Response: A section on molnupiravir has been added to the manuscript on page 17-18..

vi - Bromhexine as the drug with the strongest inhibitory effect on TMPRSS2. It can be used to block pulmonary virus infection, A large number of sticky secretions have been seen in the autopsy lung sections of COVID-19 patients who have died.

Response: A section on bromhexine has been added to the manuscript on page 6-7..

3 - As regard COVID-19 vaccines and chronic liver diseases :there is no specific side effects or complications , the discussion is vague not give any specific conclusions e.g reference 119 page 19 (Each study group included 596618 persons, and the vaccinated population included 9699 (1.6%) patients with liver disease and 435 (0.1%) patients with solid organ transplantation [119].???? where the results of the study as regard these liver group??

Response: Published data on COVID-19 vaccines in specific patient subgroups is currently very limited. The investigators have performed a number of additional subgroup analyses, each time restricting the matching process to persons with a specific condition of interest, in order to maximize the sample size., but the results on the liver disease subgroup are not yet known. The discussion part has been lengthened and the reviewer' recommendations included.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The present study was well organized or reviewed adverse GI symptoms or hepatic injury related to COVID-19 treatment drugs and vaccines. The treatment drugs and vaccines for COVID-19 give a lot of information for us.

(1) ***Science editor:*** 1 Scientific quality: The manuscript describes a review of the gastrointestinal and hepatic side effects of potential treatment for COVID-19 and vaccination in patients with chronic liver diseases. The topic is within the scope of the WJH. (1) Classification: Grade B and Grade B; (2) Summary of the Peer-Review Report: The submitted article is valuable. The present study was well organized or reviewed adverse GI symptoms or hepatic injury related to COVID-19 treatment drugs and vaccines. However, there are still some minor issues that need to be corrected. The questions raised by the reviewers should be answered; (3) Format: There are 3 tables; (4) References: A total of 138 references are cited, including 79 references published in the last 3 years; (5) Self-cited references: There is no self-cited reference; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B and Grade B. 3 Academic norms and rules: The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. The topic has not

previously been published in the WJH. 5 Issues raised: (1) Please write the "Conclusion" section at the end of the main text. 6 Recommendation: Conditionally accepted.

Response: A conclusion has been added at the end of the main text on page 29-30.

(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 Hepatology, 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.

The manuscript was revised according to reviewers' and editors' recommendations.

We hope that, with these revisions, the article is now suitable for publication in World Journal of Hepatology. I look forward to hearing from you soon.

Yours sincerely,

Dr Man Fai Law