

Dear Dr. Lian-Sheng Ma

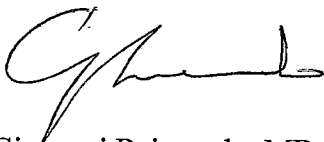
Thank you for the opportunity to publish a paper in WJG.

In this context, I would like to summarize what happened in the past five months:

- In June 2013 the Editor of WJG kindly invited me to write a review entitled: Hepatitis B virus and hepatitis C virus dual infection
- After a few days, I accepted the invitation
- On 29<sup>th</sup> October 2013, together with my coworkers GC and FS, we submitted the paper
- On 20<sup>th</sup> January 2014 you invited us to re-submit the manuscript according to the suggestions of four reviewers, three of whom provided a very positive evaluation whereas the fourth suggested that the review should be rejected
- You gave us 3 weeks to send the revised manuscript, but the web-site of the Journal was out of order for several weeks.
- Consequently, we didn't have the chance to read the comments of the reviewers with sufficient attention until the last few weeks
- We are now submitting the new version of the paper revised in accordance with the suggestions of the three reviewers who appreciated the paper. Actually, we have provided point by point answers also to the criticisms of the fourth reviewer who expressed the unfavorable judgment.

Please, let us know at your earliest convenience if the paper can now be definitively considered accepted for publication.

Best regards



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Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 6945-review.doc).

**Title:** Hepatitis B virus and hepatitis C virus dual infection

**Author:** Gaia Caccamo, Francesca Saffioti & Giovanni Raimondo

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 6945

The manuscript has been improved according to the suggestions of reviewers: following the point by point answers to the reviewer's comments

Reviewer 00199533

We are sincerely grateful to the reviewer for the very positive general evaluation and kind comments about our paper. Indeed, he/she did not request any revision of the paper.

Reviewer 01716622

We are sincerely grateful to the reviewer for the positive evaluation of our paper. We corrected the typo in the Introduction line 2 ("considerable")

Reviewer 02567528

We are sincerely grateful to the reviewer for the positive evaluation of our paper.

1. As suggested, we have modified the sentence (new version: "integration is possibly a cofactor related to the development of HCC") and we have cited two additional reviews concerning HBV-related hepatocarcinogenesis (new references n. **41**: Neuveut C, Wei Y, Buendia MA. Mechanisms of HBV-related hepatocarcinogenesis. J Hepatol. 2010 Apr;52(4):594-604. and **42**: Pollicino T, Saitta C, Raimondo G. Hepatocellular carcinoma: the point of view of the hepatitis B virus. Carcinogenesis. 2011 32:1122-32)
2. We have replaced "dates back to" by "goes back to being"
3. As suggested, we have cited the paper by Huang et al (Huang YT et al, J Clin Oncol 2011; 29: 3643-50; new reference n.102). Moreover, we have moved the previous citation n. 98 (Aghemo A, Colombo M. Treatment of patients with dual hepatitis B and C: a step in the right direction. Gut 2014; 63: 380-1) to a section of the paper concerning the therapy (new reference n.105).
4. We have corrected the typos in table 2. We have also carefully evaluated the reviewer's suggestion of indicating the values in the last three columns of the table as percentage of

response. Nevertheless, this is very difficult for the heterogeneity of the examined populations. In any case, we revised the table and inserted the values not as percentage but as number of patients corresponding to the categories indicated in the corresponding last three columns (HBV DNA detectable at baseline, HBV DNA disappearance after therapy, HBV DNA reappearance after therapy).

5. We have corrected table 1 as regards reference 11
6. The typos throughout the text have been corrected.

Reviewer 02528622

- The term "quasispecies" to refer to intrahost HCV genetic variability has been used in this text according to P. Farci. We introduced the term in the text and cited the reference (Farci P. New insights into the HCV quasispecies and compartmentalization. Semin Liver Dis. 2011; 31: 356-74).
- The immunological aspects associated with the dual infection by HBV and HCV are not yet clarified and the clinical studies analyse very few cases, thus they could be considered anecdotal. For this reason they were not discussed before in our paper. Nevertheless, following the reviewer's suggestion we inserted a new sentence in the text in this context ("The immunology of the HBV-HCV dual infection has been evaluated in a few studies focused on T-lymphocyte response and analyzing small numbers of cases. Larger studies are needed to better clarify the complex immunological aspects of this condition") and cited two immunological studies conducted in cases of HBV and HCV dual infection (new reference number 78 and 79).
- In the previous version, we had already cited eight papers concerning the possible outcome of the double infection, papers that were cited at the end of the text section. In the revised version, we have included additional references and distributed them in the different parts of the section.

Best regards



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