Response to Review Comments

| Manuscript Title | Current status of first-line therapy, anti-antiogenetic therapy and its combinations of other agents for unresectable hepatocellular carcinoma | |
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| Manuscript Number | 64343 | |
| Journal | World Journal of Gastrointestinal Oncology | |
| Authors | Saleh A. Alqahtani, Massimo Colombo | |
| Comments Received | 15 Mar 2021 | |
| Revision Submitted | 24 Mar 2021 | |

| S. No. | Section / Content | Comment | Response | |
|----------|-----------------------|---|--|--|
| Reviewer | Reviewer 1 | | | |
| 1 | General / Language | This review paper is interesting. I have no other comment. But, minor language polishing is needed. | Thanks for the comment. We have subjected the manuscript to language polishing to make it read better. English editing certificate has been attached separately. | |
| Reviewer | Reviewer 2 | | | |
| 2 | General / Language | This is a revised version review on therapeutic drugs for unresectable HCC. The manuscript is concisely reviewed and well written. I only point out some mistakes as follows: 1. p10 line19 real-life world → real-world 2. p15 line7 partialresponse → partial response 3. p16 line6 progressive → progression | Thank you very much for the comment. We have made all the changes. | |

| S. No. | Section / Content | Comment | Response |
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| Reviewer | 3 | | |
| 3 | Lenvatinib failure | Thank you for your great thesis. I'd like to ask you one point. | Thanks for your viewpoint. We have included the following texts on page 16: |
| | | I'd like to have a reference to the secondary drug after the first targeted treatment failure. I think regorafenib, cabozantinib will need to comment. Thank you for your hard work. | "As of date, there are no standard treatment options available for patients who encountered lenvatinib failure. Sorafenib can be considered in such cases, given that about one-fourth of patients in the REFLECT trial received sorafenib while taking lenvatinib as the first-line medication ^[38] . Recently, a Japanese pilot study has suggested the potential therapeutic benefit from ramucirumab after lenvatinib failure in HCC patients; nevertheless, another study with more patients could not confirm such benefits in the post-progression treatment ^[39,40] ." |
| Science E | ditor | | |
| 4 | Author Contributions Section | The "Author Contributions" section is missing. Please provide the author contributions | Thanks for the comment. We have now added the authorship contributions and other relevant sections stated in the guidelines and requirements for manuscript revision. |
| 5 | Language evaluation | Classification: Grade A and two Grades B. No language editing certificate was provided. | Thanks, the English editing certificate has been attached separately. |

| S. No. | Section / Content | Comment | Response |
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| 7 | References | PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout | Thanks for the comment. We have included PMID and DOI (wherever applicable) in references. |
| 8 | References | Please revise the references according to the Format for references guidelines, and be sure to edit the reference using the reference auto-analyser. | The references have been updated in accordance with the format for references guidelines of the journal. |

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| 10 | Manuscript Information | Please check if the manuscript information is correct. | Thanks for the comment. We have thoroughly checked for the accuracy of information provided in the manuscript. |
| 11 | Footnotes and Figure Legends | The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor (a) Requirements for figures: Please provide decomposable Figures (whose parts are all movable and editable), organize them into a single PowerPoint file, and submit as "64343-Figures.ppt" on the system. The figures should be uploaded to the file destination of "Image File". (b) Requirements for tables: Please provide decomposable Tables (whose parts are all movable and editable), organize them into a single Word file, and submit as "64343-Tables.docx" on the system. The tables should be uploaded to the file destination of "Table File". | The figure and table (1 each) have been moved out of the manuscript file and submitted separately as suggested: Figure in PPT & table in Word files. |
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| 13 | Conflicts of | Please download the fillable ICMJE Form for | ICMJE Form for Disclosure of Potential Conflicts of |
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