

São Paulo, July 21^h, 2022

Letter to Editorial Board of the World Journal of Gastrointestinal Surgery

Point-by-Point Answers for the Reviewers

REF.: 77473 - Is There a Role for Surgery for Colorectal Liver Metastases Progressing during Chemotherapy?

Dear Editors and Reviewers,

First and foremost, thank you so much for inviting me to write a manuscript for the World Journal of Gastrointestinal Surgery, and as a member of this Editorial Board, I would like to state that I appreciate the invitation and we prepared the manuscript to fit as a Minireview according to the journal requirements for this category.

Thank you all for completing the examination of our manuscript.

We have prepared a revised version addressing all the issues raised by the reviewers. We have carefully gone through the manuscript to make the appropriate changes in the text (highlighted in **yellow**). Moreover, all answers for the reviewers are answered below, point-by-point. We hope that our article will be suitable for this prestigious journal.

Sincerely,

Raphael Araujo

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors provide a great review detailing the integration of surgery with chemotherapy for treatment of colon cancer metastatic to liver.

1) The authors spend a great deal of time discussing management of metastatic colon cancer with mets to the liver. The title of the manuscript however is: Is There a Role for Surgery for Colorectal Liver Metastases Progressing during Chemotherapy? As the title only pertains to the last section of the manuscript, would change the title to better describe the full content of the manuscript

Answer: Thank you so much for your meaningful comment. The initial idea was to deal with this arid subject by addressing the challenges of clinical practice. Thus, we wrote the paper exposing the most important aspects that are necessary for a multidisciplinary decision to indicate or refuse surgery for patients with CRLM progressing during chemotherapy.

2) Ref 16 was used in the section 'perioperative chemotherapy in initially resectable patients' should quote the numbers in the manuscript, pertaining to overall survival characteristics in both groups

Answer: Thank you so much for this remarkable suggestion, we appreciate it.

Sentences addressing this piece of information about Overall Survival were added and highlighted in this section.

3) In the section 'perioperative chemotherapy in initially unresectable patients', some sentences to describe the complications of bevacizumab towards surgical outcomes should be mentioned.

Answer: Thank you for this suggestion, we agree with you and this important piece of information was missing in the manuscript. We added sentences addressing the addition of bevacizumab to chemotherapy and its association with a higher incidence of treatment-related complications.

Moreover, we also added in the role of surgery sections that an interval of at least 6 weeks between the last dose of bevacizumab and elective surgery is usually recommended to mitigate the risk of complications. Nevertheless, its postoperative use should be delayed at least 6 to 8 weeks after surgery. Thank you so much for the attentive review and meaningful suggestions, they improved our manuscript.

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade A (Priority publishing)

Conclusion: Rejection

Specific Comments to Authors: The authors summarize the surgical treatment strategies for CRLM, and focuses on a problem that is widely concerned in the

industry: Is there a role for surgery for colorectal liver metastases progressing during chemotherapy? It is maybe helpful for clinicians to make decision for treatment strategies. However, the article lacks internal logic, and there is no clear logical chain between and within each sub-theme, making it difficult for readers to obtain sufficiently clear research conclusions. The article seems to simply follow the main content of the current international guidelines/standards for the diagnosis and treatment of CRLM in major countries/regions. It does not provide opinions and conclusions about the updated research progress of CRLM, thus cannot provide better help for clinicians to formulate treatment strategies. For the most important theme of this article, the Role for surgery for CRLM progressing during chemotherapy, the authors did not effectively summarize the existing relevant research according to the pros and cons viewpoints, so the readers could not clearly identify the clinical research results for supporting or opposing this specific question.

Answer: Thank you for your attentive review, we do appreciate the opportunity to overcome part of the drawbacks and limitations of our study with your valuable contributions. They are increasing our manuscript's quality, and sentences addressing changes are highlighted in the text.

Indeed, the CRLM surgery during chemotherapy interests the industry, however, we do believe that no more than surgeons dealing with digestive surgical oncology, especially in a multidisciplinary decision manner, mainly in tumor boards, as expected for good standards of practice in oncology. Considering the difficulty of this subject, we proposed this paper addressing the controversies as frontiers in GI oncology that

claimed to be explored in a multimodal approach for both medical and surgical oncologists either in medical or surgical periodicals.

We understand and appreciate your concerns about the lack of our opinions and suggestions, but we assumed that it would not be appropriate for frontier or minireview articles based on the Journal's Guidelines for Manuscript Preparations * (as demonstrated as a footnote) on to these modalities. As a result, we avoided imprinting our opinion as much as possible without any support in the literature, despite the paucity of literature on this subject. However, some opinions are inherent in a narrative review model, or a minireview, when the data is chosen based on the author's judgment and preference, rather than through a systematic search and review. We made some changes to the text to address these points in the text. We appreciate your keen insight, and we believe it helped to improve our manuscript.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: No specific comments

Answer: Thank you so much for your time and consideration in reviewing our manuscript, we appreciate it.

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Guidelines for Manuscript Preparation and Submission

Core tips according to the modalities

Frontier: Highly influential scientists are invited to write Frontier articles by selecting a highly cited, cutting-edge original paper of his/her own and summarizing the major findings, the problems that have been resolved and those that remain to be resolved, and the future research directions in order to help readers understand his/her important academic point of view and perspectives on the directions of research in their field.

Minireviews: Highly influential scientists are invited to write Minireview articles on recent advances and trends in molecular biology, genomics, and related cutting-edge technologies to provide readers with the latest knowledge and to help improve their diagnostic and therapeutic skills.