

July 29th, 2021

Prof. Hiten RH Patel, BM BCh, BSc, FRCS, PhD & Prof. Stephen Safe, PhD

Editors-in-Chief

World Journal of Clinical Oncology

We are pleased to re-submit for publication our review article titled: *"The role of liver transplantation in the management of colorectal liver metastases: challenges and opportunities"*.

We are grateful to the editors and reviewers for providing insightful feedback on our study. We have carefully reviewed the recommendations and have revised our manuscript accordingly. Addressing each of their comments has certainly improved our manuscript. Detailed responses to the reviewers' comments are provided below.

Reviewer 1:

Comment: *"This paper is carefully treating a review about the role of liver transplantation in the management of colorectal liver metastases. This is a well written, interesting, and useful contribution, which I think is entirely suitable for publication in WJCO. Although I have no doubt about the quality of the presented work, I recommend to make a list of all past studies' information about liver transplantation for colorectal liver metastases in the section of "recent era" so that the readers can follow easily"*

Response:

We thank the reviewer for this comment. We added Table 1 that reports the study characteristics and findings of the early experience and recent era studies.

Reviewer 2:

Comment: *"The present study is an excellent review of the current perspective of LT for unresectable colorectal liver metastasis confined to the liver. The authors have covered all the fields starting from the historical perspective to the current criteria for patient selection. My only criticism is regarding the immunosuppression following liver transplantation for CRLM. As far as my knowledge the effect of chemotherapy has not been to be a negative factor following LT. However, there is an ambiguity. A reorganization of this section would strengthen this study."*

Response:

We appreciate the reviewer's input. Indeed, we start this section by stating:

"Immunosuppression is a controversial topic..."

We modified the section to further clarify the ambiguity of the immunosuppression in transplanted patients for underlying malignancy:

"...That is because attenuation of the native immune response from immunosuppression is essential to prevent graft rejection, however, it may contribute to unfavorable post-LT outcomes in patients with disseminated malignant disease, as it could facilitate disease recurrence."

Additionally, this section closes by stating:

"However, the current level of evidence is relatively low, and future high-quality studies are required to draw solid conclusions for immunosuppressive therapies after LT for CRLM."

Editorial office

Science editor: *"Please correct manuscript based on Peer-Review reports and issues raised. Afterwards, the manuscript can be reconsidered."*

Response:

We have carefully reviewed the recommendations and have revised our manuscript accordingly. Addressing each of their comments has certainly improved our manuscript.

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 Clinical Oncology, 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."*

Response:

We hope that with these revisions, our work is felt appropriate to publish in *World Journal of Clinical Oncology* and perceived as educational to the Journal's readership. Thank you again for inviting us to submit the second revision our work to your journal. We would be pleased to answer any additional concerns or questions you may have.

Sincerely,

Georgios Tsoulfas, MD, PhD, FICS, FACS,

Associate Professor of Surgery

Department of Transplant Surgery, Aristotle University School of Medicine, 66 Tsimiski Street, Thessaloniki 54622, Greece

Email: tsoulfasg@gmail.com

Telephone: +306971895190