

Dear Editor,

Enclosed please find the revision of our manuscript entitled “Re-evaluating the Role of Pelvic Radiation in the Age of Modern Precision Medicine and Systemic Therapy”.

After the help from the BPG Help Desk, we had successfully uploaded the files needed except the revised manuscript file. Therefore, we submitted the revised manuscript file as the Supplementary Material “88390-Supplementary Material-revision.docx”

In this revision, we have revised the issues raised by the reviewers. Changes we made to our manuscript were highlighted in yellow so the reviewers can easily see the changes. We hope that we have sufficiently addressed the reviewer’s comments, and look forward to hearing your decision regarding the paper.

Sincerely,

Chun-Ru Chien, M.D. Ph.D.

Professor, School of Medicine, College of Medicine, China Medical University

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The authors made a careful summary of evidence supporting the neoadjuvant systemic therapy without radiation. So far, no solid data has been achieved that only chemotherapy could take the place of chemoradiation, especially in locally advanced diseases (such as mrMRF+, or N2, or EMVI+).

#A1. In response to comments from reviewer #1.

. We thank for the remind from the reviewer that the use of chemotherapy only was less suitable for patients with the above mentioned high risk features. These were addressed in the revised manuscript [see highlight in 1st paragraph of “Text”]

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The title includes pelvic radiotherapy, but the authors

only mentioned pelvic radiotherapy in locally advanced rectal cancer under this title. They presented chemotherapy and surgery as a clear treatment option for locally advanced rectal cancer, but the group that can be treated with chemotherapy and surgery alone is still very limited in the guidelines. In order not to give the wrong message to the reader, I think it would be a more accurate message if the patient group was defined as, for example, if the response to chemotherapy is >20%, there is a surgery option without RT. In addition, immunotherapy is recommended in some groups for rectal cancer, but this issue is not mentioned at all. The table is not understandable, it should be edited. Additionally, p values for the studies should be given.

#A2. In response to comments from reviewer #2.

@ A2.1. We agree with the reviewer that the use of systemic therapy was limited to certain population. These were addressed in the revised manuscript [see highlight in 1st paragraph of "Text"]

@ A2.2 . The whole manuscript (including the table) had been edited by a professional English language editing company (see certificate) to improve its clarity. P values were added in the table.

(1) Science editor:

The manuscript has been peer-reviewed, and it is ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade D (Fair)

#A3. In response to comments from Company editor-in-chief

(2) Company editor-in-chief:

I recommend transfer to World Journal of Clinical Oncology. I have reviewed the Peer-Review Report and the full text of the manuscript, 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. The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for

the professional English language editing companies we recommend:
<https://www.wjgnet.com/bpg/gerinfo/240>. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>. Uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

@ A3.1 The manuscript had been edited by a professional English language editing company (see certificate)

@ A3.2 We had visited the RCA database to search from the keywords in our manuscript (radiotherapy; locally advanced stage rectal cancer; precision medicine; systemic therapy; clinical trial) but found no highlight articles.

@ A3.3 There were not figures in our manuscript.