

Author's Responses to the Reviewers' and Editors' Comments

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO: 81519

Title: Implications of recent neoadjuvant clinical trials on the future practice of radiotherapy in locally advanced rectal cancer

I appreciate the useful and relevant comments made by the reviewers and editors. Having revised my manuscript according to their comments, I herein provide my answers to the comments with explanations of the corrections/additions.

While revising my manuscript, I focused on the following aspects according to the editorial office's comments: (1) refining the manuscript, (2) addition of new references to improve the content of the manuscript, (3) correction of the format of the manuscript to meet the guideline and requirements of the *World Journal of Gastroenterology*, and (4) language polishing.

All changes are highlighted in yellow in the manuscript and important changes are explained below. All other changes are the results of language polishing or paraphrase to clarify the meaning of the sentences. I believe that the revised version will meet the journal publication requirements.

Refining the manuscript

- (p5) To clarify the meaning of the sentence, I revised it as follows.

before: Several early-phase clinical trials have reported a higher response rate to neoadjuvant treatment combined with ICIs for LARC than that to conventional CRT, whose treatment protocols and important findings are summarized in Table 2 and Supplementary Table 1.

revised: Several early-phase clinical trials have reported higher response rates to neoadjuvant treatment combined with ICIs for LARC, when compared to historical rates with conventional CRT. Their treatment

protocols and important findings are summarized in Table 2 and Supplementary Table 1.

- (p9) To clarify the meaning of the sentence, I revised it as follows.

before: However, the added value of RT combined with ICIs needs to be explored in patients with dMMR LARC with varying tumor burdens when considering the association between tumor burden and the response to immunotherapy^[73].

revised: However, in dMMR LARC with high tumor burden, immunotherapy alone may be insufficient to eliminate all the tumor cells in the body when considering the association between tumor burden and the response to immunotherapy^[73]; therefore, the combination of RT and immunotherapy may be needed for dMMR LARC.

Addition of new references

- (p4) I found one article which was published after I submitted my manuscript through searching the new information related to my manuscript via RCA and other searching tools. An institutional paradigm for total neoadjuvant therapy for LARC by Roeder *et al*, published in November 2022, was added to the manuscript.

before: Based on the results of the aforementioned RCTs of TNT, Hui *et al*^[28] introduced ...

revised: Based on the results of the aforementioned RCTs of TNT, Hui *et al*^[28] and Roeder *et al*^[29] introduced ...

- (p9) Retrospective studies were added to provide more information.

before: The trial by Cercek *et al*^[19] supports the use of immunotherapy alone for dMMR LARC.

revised: Extremely high response rates to immunotherapy alone, shown in retrospective^[72] and prospective^[19] studies, support the use of immunotherapy alone for dMMR LARC.

Format of the manuscript

- Abbreviations
 - (p2) In Abstract, “RT” was replaced with “radiotherapy”.
- Tables
 - All tables (Table 1, Table 2, and Supplementary Table 1) were revised to have only three lines according to the journal’s guideline. The name of the 1st column (Trials) was added.

Language polishing

- I carefully revised the manuscript and requested language editing service by Editage again.