Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-23-1333

Reviewer A

The abstract provides interesting insights into a study on combining radiotherapy with pembrolizumab and bevacizumab for advanced hepatocellular carcinoma (HCC). However, it could be improved by providing a more detailed background, clarifying the significance of the findings, addressing limitations, and discussing practical implications for clinicians and researchers. The small sample size and retrospective nature of the study should also be acknowledged.

Reply: There are three concerns: (i) improve abstract by providing a more detailed background; (ii) clarify significance, limitations, implications; (iii) acknowledge small sample size and retrospective nature.

(i) The PD-1/PD-L1 inhibitor plus bevacizumab has been established as first-line systemic treatment for advanced hepatocellular carcinoma; radiotherapy is one of the most common local treatment approaches. Preclinical research result that radiotherapy enhances efficacy of anti-angiogenesis treatment plus immunotherapy has not yet been confirmed in clinical practice. Whether patients with advanced hepatocellular carcinoma benefit from combing radiotherapy with pembrolizumab and bevacizumab remains unclear. These are the reasons why this study has been carried out. We have modified the background of the abstract (see Page 2, line 35~42).

(ii) This study firstly reported that combining radiotherapy with pembrolizumab and bevacizumab was preliminarily a feasible and effective therapeutic choice for advanced hepatocellular carcinoma in despite of more treatment-related adverse events (significance of this study, see Page 3, line 60~62). This tri-modal regimens may be a potential conversion therapy for unresectable, locally advanced hepatocellular carcinoma (implication of this study, see Page 3, line 62~63). The limitation of this study are its retrospective nature and small sample size (limitation of this study, see Page, line 63~64).

(iii) The retrospective nature and small sample size have been acknowledged in abstract (see Page 3, line 63~64) and the discussion part of main text (see Page 13, line 308).

Reviewer B

1. HBV/HCV/CRT/ATP/HMGB1/cGAS/STING/PR/SD/CR/DC should be defined upon first use in the Main Text.

Reply: HBV and HCV (see Page 5, line 76), CRT (see Page 5, line 100), ATP (see Page 5, line 100-101), HMGB1 (see Page 5, line 101), cGAS (see Page 6, line 104), STING (see Page 6, line 105), PR (see Page 9, line 194), SD (see Page 9, line 194), PD (see Page 9, line 194), CR (see Page 9, line 193), DC (See Page 11, line 254).

2. All genes in the manuscript should be italicized.
Reply: All genes have been italicized.

3. Where “Response Evaluation Criteria in Solid Tumor (RECIST) v 1.1.” is first mentioned, a citation is needed.
Reply: The citation has been added on Page 7, line 149 (also see Page 16, line 397~398).

4. ORR/OS/DCR/TRAEs/DAMPs are defined more than once in the Main Text. They should only be defined on first use.
Reply: All duplicate definitions have been deleted.

5. “our study cohort” is suggested to be replaced with “our cohort study”.
Reply: See Page 11, line 273.

6. All the abbreviations in the figure(s) and table(s) should be defined in the explanatory legend.
Reply: See attached file named “Tables-revised” and figure legends in the manuscript (Page 14, line 344~356).

7. Subfigures should be named using alphabets. Please update Figure 3 along with its citations.
Reply: See attached file named “Figure 3” and the text in the manuscript on Page 9, line 199~200 and Page 14, line 348~349.

8. Table 1: “All (%) (n=23)”, not all of the values are presented as percentage. Please add percentage to the row headers instead of the column header.
Reply: See attached file named “Tables-revised”.