

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 81122

Title: Correlation between immune-related adverse events and long-term outcomes in pembrolizumab-treated patients with unresectable hepatocellular carcinoma: A retrospective study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05230210

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2022-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-26 10:11

Reviewer performed review: 2022-11-08 15:12

Review time: 13 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
statements	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors for their important work. Here I have some comments:

Title is relevant Abstract: good Add to the conclusion a note on the survival. You only state a “a better therapeutic effect.” Although the results mention a better OS. Keywords: kindly add Pembrolizumab by name. Please modify HCC to unresectable or advanced HCC. Introduction: 1- The authors mentions “Locoregional therapy including radiofrequency ablation (RFA),” as one of the treatments, but I think it is more beneficial to mention resectable versus unresectable or curable versus advanced, as RFA is one of the curative measures. RFA should not be mentioned here for comparative survival except if used for the downgrading of the tumor. 2- in line 103: “autoimmunelike” please correct to “autoimmune-like” Methods: 1. The authors mentioned “evaluation criteria in solid tumors criteria (mRECIST) every 3–6 weeks by contrast-enhanced CT or MRI examination.”>>> does that mean for the whole duration of follow up ie two years, because the radioactive exposure will be very high. Kindly elaborate. 2. The authors wrote “imageological”>>this could be a hard word, could you use a more common one like “imaging study”. 3. Could the authors state the longest duration of follow up? (example the longest FUP was two years or 24 months) to make clear that OS here is a short one. You stated that later in days which may be confusing to the reader. 4. There is no mention of AFp and whether it was used in FUP, although it is mentioned in results of univariate analysis. Results: 1. The univariate and multivariate analysis presents all factors like a correlation table, could you kindly modify the table to contain the most relevant factors (max 5-6) especially in the multivariate analysis or separate the tables. 2.

It is not clear if the base child pugh had a direct effect on the occurrence of adverse events or whether it changed on follow up, could you kindly clarify? 3. The effect of the tumor burden and drug response on AFP, could you mention in more details? Discussion: The authors concentrated on the effect of the drug on hypothyroidism and its relation to response rate. However, there is no mention of the effect of the drug on OS and the difference from the previous RCT conducted, and whether the multivariate factors detected in the statistical analysis are different from previous studies. Kindly add to discussion. Conclusion: the conclusion at the start of the manuscript is the same as the end, please rewrite, as they have to be different. Also add future aspiration in the research in this area.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03739641

Position: Editorial Board

Academic degree: PhD

Professional title: Nurse, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2022-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-03 07:35

Reviewer performed review: 2022-12-07 02:36

Review time: 3 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
statements	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I appreciated getting a chance to review your valuable manuscript. 1. At figure 1, you wrote mTECICT should be written mRECIST. Please check and revise here. 2. In Figures 2 and 4, you wrote rat in the y-axis, those should be written in rate. Please check and revise those. 3. In figure 3, why you did not include progression disease cases? Were there no irAEs in PD cases? Please check and revise here. 4. In figure 4, how many cases are included this spider plot? It did not include the 99 cases, you mentioned in figure 3 legends. Please check and revise here. 5. Figure 4 looks complicated due to the differences in the colors. You should use the same color as the line bar and symptom. Please check and revise here. 6. The number of cases with hypothyroidism was relatively small. So, that is a big limitation of this study. You already mentioned it in the limitation part. But, please check and revise that sentences.