



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 46708

Title: Optimizing radiotherapy with immune checkpoint blockade in hepatocellular carcinoma

Reviewer’s code: 02992848

Reviewer’s country: Taiwan

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-03-12 00:43

Reviewer performed review: 2019-03-13 07:17

Review time: 1 Day and 6 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting manuscript concerning role of radiation therapy on immunotherapy for hepatocellular carcinoma. Therefore, this manuscript will add to growing body of literature on the use of Immunotherapy and radiation therapy in the



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treatment of HCC. There are a few issues in the manuscript that need to be addressed prior to publication, and I recommend making the following clarifications before publishing this paper. Nevertheless, it should be published. 1. Hope the authors can provide more clinical data concerning the benefit of concurrent ICI and radiation therapy in clinical practice, as this can make this prospective treatment more convincing.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
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- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 46708

Title: Optimizing radiotherapy with immune checkpoint blockade in hepatocellular carcinoma

Reviewer's code: 02936822

Reviewer's country: France

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-03-12 07:42

Reviewer performed review: 2019-03-20 20:06

Review time: 8 Days and 12 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors propose a timely, comprehensive and balanced overview of the use of ICI, EBRT and their combination in HCC. I have only minor comments: 1- In the introduction, the authors stated: "The surgical removal of tumors and elimination of



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cancerous cells by chemotherapy or radiotherapy are no longer the best options, but rather, the reinvigoration of the antitumor immunity that is suppressed or exhausted in the tumor microenvironment (TME) is now more appealing." Surgery and radiotherapy are still the main curative treatment of solid tumors. Please amend. 2- In the ICI section, the authors stated: "The efficacy and safety of combination treatment with PD-1 and CTLA-4 inhibitors in patients with HCC have been proven in phase I/II trials" I would recommend rephrasing that: while safety can be proven in phase I/II, efficacy should be proven in phase 3. Please cite the recent press release about the Phase 3 Keynote 240 of pembrolizumab ; please cite the waiting of the Checkmate-459 with nivolumab. 3- EBRT in HCC section: ref 45 is inadequately quoted: the BCLC does not support use of EBRT. The only reference to radiation therapy in the paper referenced in 45 is "Arterial embolisation without chemotherapy, external radiotherapy, and radioembolisation have shown antitumour activity, but survival benefit has not been proven." Please amend, stating that the BCLC does not include EBRT as a main treatment modality for HCC. You could also present more recent recommendation (EASL, but certainly interestingly to your topic asian guidelines). 4- The authors partially discuss the potential study of SIRT. I would be interested that the authors give some insight about the difference in radiobiology between EBRT and SIRT. In the fractionation section, the authors clearly showed the accumulating evidence for more immunogenic effect of hypofractionation. SIRT is rather an hyperfractionation...

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No

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[Y] No