

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47938

Title: Is the treatment outcome of hepatocellular carcinoma inferior in elderly patients?

Reviewer's code: 03473536

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-01 17:11

Reviewer performed review: 2019-04-07 10:31

Review time: 5 Days and 17 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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Comment to the Authors Dear Dr. Chu, thank you for submitting your manuscript entitled "Is the treatment outcome of hepatocellular carcinoma inferior in elderly patients?". The paper is well written and surely gives new ideas in the therapeutic evaluation of such complex patients. I think your paper is suitable for publication.



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INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47938

Title: Is the treatment outcome of hepatocellular carcinoma inferior in elderly patients?

Reviewer's code: 02959077

Reviewer's country: France

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-04 21:57

Reviewer performed review: 2019-04-07 21:06

Review time: 2 Days and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" 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 checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review is clear, based on a pertinent choice in the literature. Some data may be discussed nevertheless: - evolution in HCC epidemiology through ages and after 80 years particularly (decrease in HCC incidence after 80 years?); - some data were published concerning ethanol injection, even if this treatment was not frequent; - few data concerned other general therapies than sorafenib in advanced HCC when some old patients are



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included. **REPLY:** The following sentence is added to the 3rd paragraph: "The incidence rate of HCC raises at the age of forties and decreases after eighties^[6]." (A reference added)
In the section RADIOFREQUENCY ABLATION, the following text is added:
"Percutaneous ethanol injection has been used to treat elderly HCC patients but evidence of its efficacy is limited^[70, 71]. RFA has largely replaced percutaneous ethanol injection for better recurrence-free survival and fewer treatment sessions^[72]." (3 references added)

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47938

Title: Is the treatment outcome of hepatocellular carcinoma inferior in elderly patients?

Reviewer's code: 02861372

Reviewer's country: Egypt

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-01 09:52

Reviewer performed review: 2019-04-18 13:13

Review time: 17 Days and 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" 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 checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear Authors This is an important review article about management of HCC in elderly population. Thank you for the clear simple language.

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? **yes**

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript?
yes

3 Key words. Do the key words reflect the focus of the manuscript? yes

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? yes

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? yes

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? It is a good review for physicians working in HCC multidisciplinary clinics for management of HCC in elderly patients. It summarizes all what was published in the literature about this issue.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently?

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends?

9 Biostatistics. Does the manuscript meet the requirements of biostatistics?

10 Units. Does the manuscript meet the requirements of use of SI units?

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? They cite appropriate references

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? The manuscript is well organized. the style, language and grammar

are accurate and appropriate

13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting?

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? **yes**

Comments to the authors: **Regarding targeted therapy: You mentioned that: morbidities including neutropenia, malaise and mucositis occurred more frequently in elderly patients. Dose reduction is a way to increase its tolerability What about hand and foot syndrome and diarrhea in the elderly? Were they increased too?** **REPLY:** The following text is added: "Other common adverse effects (e.g. hand and foot syndrome and diarrhea) were reported to be similar in both populations^[80]." (The study by Wong et al. is cited here.) **Is there a difference in survival between elderly and nonelderly after Sorafenib treatment?** **REPLY:** The second sentence in that section is revised to "It has been reported that sorafenib achieved similar progression-free survival and overall survival in elderly and young patients with advanced HCC." **You mentioned that: Despite limited data, immune checkpoint inhibitors represent a potential option of nonsurgical treatment for elderly HCC patients. Was this mentioned in the literature with a possible reference? Or this is your recommendation?** **REPLY:** In the CheckMate 040 study, 42% of patients



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were 65 or older in the escalation phase, and 47% of patients were 65 or older in the expansion phase, but the effect on toxicity and functional status is unknown in these fit, older HCC patients. The word “may” is added to the mentioned sentence: “...immune checkpoint inhibitors *may* represent a potential option...”, and a reference (study by El-Khoueiry et al.) is added.

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