

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65904

Title: Trial eligibility in advanced hepatocellular carcinoma: does it support clinical practice in underrepresented subgroups?

Reviewer's code: 03550692

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Argentina

Manuscript submission date: 2021-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-19 10:26

Reviewer performed review: 2021-03-22 13:19

Review time: 3 Days and 2 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 Grade E: Do not publish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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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 statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The inclusion criteria used in clinical trials do not support the use of novel therapies in several real-world scenarios involving underrepresented subgroups, such as patients with unpreserved liver function, other comorbid conditions, a history of solid-organ transplantation, auto-immune disorders and those with a high risk of bleeding. This article discussed treatment strategies in these subgroups and is of promotional significance to improve the level of HCC treatment. It is recommended to publish.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65904

Title: Trial eligibility in advanced hepatocellular carcinoma: does it support clinical practice in underrepresented subgroups?

Reviewer's code: 00051373

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: Argentina

Manuscript submission date: 2021-03-17

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-04-13 12:38

Reviewer performed review: 2021-04-14 13:43

Review time: 1 Day and 1 Hour

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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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 statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Thank you very much to let me for reviewing this comprehensive review which was described the overall systemic treatment options in first and second line treatment in for the advanced hepatocellular carcinoma. Manuscript is well preparation and written well.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65904

Title: Trial eligibility in advanced hepatocellular carcinoma: does it support clinical practice in underrepresented subgroups?

Reviewer's code: 03476225

Position: Peer Reviewer

Academic degree: MD

Professional title: Consultant Physician-Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: Argentina

Manuscript submission date: 2021-03-17

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-04-13 14:58

Reviewer performed review: 2021-04-19 07:12

Review time: 5 Days and 16 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 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 statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

MANUSCRIPT TO BE REVIEWED: Trial eligibility in advanced hepatocellular carcinoma: does it support clinical practice in underrepresented subgroups? By Federico Piñero and Leonardo da Fonseca. (Manuscript number 02993003)

GENERAL COMMENT: I enjoyed reading this paper. The authors discuss a very important topic in systemic treatment of hepatocellular carcinoma. The populations studied in clinical trials do not include lesser fit, older patients and those with important comorbidities. These patients are subject to regulatory restrictions in many countries and are often excluded from treatment. The authors thoroughly review these categories and present evidence in favor or against systemic therapy. The paper is very well written and includes the newest drugs, including checkpoint inhibitors and bevacizumab. Both the hepatologist and the clinical oncologist will find this paper very useful in their everyday practice and in choosing the right drug for the right patient. The flow charts provided in the two figures are easy to use and particularly helpful. I have only a few minor comments to improve readability and recommend publication in the Journal.

SPECIFIC COMMENTS:
INTRODUCTION: - Line 16: I suggest “no other organ failure” instead of “adequate organic function”. - Line 21: “with less than 50% liver involvement” instead of “without more than 50% of liver involvement” - Line 32 “a PDL-1 inhibitor” will be enough instead of “an ICI blocking the programmed cell-death -PD-L1- inhibition”. Everybody knows what is a PDL-1 inhibitor.
ELDERLY: - line 16: In their field-practice study Iavarone et al. found that elderly patients more frequently discontinued treatment at multivariate analysis. In these patients half dosing sorafenib was associated with increased survival while discontinuation negatively affected the outcome. This is a relevant finding and suggests that an early reduction of the dose in this population would be the best strategy. I suggest to add a comment on this point. - - line 27: do the authors suggest that an



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assessment of Clinical Significant Portal Hypertension is mandatory before starting treatment? If this is the case which tool should be used? (ultrasonography plus endoscopy would be enough? Transient Elastography?, LSPS ratio?, Baveno criteria?) FIGURES AND TABLES: - Fig.1 Lenvatinib: tumor <50% instead of > 50% - TABLE 1: MVI trunk: does it mean neoplastic PVT (Portal Vein Thrombosis)?

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65904

Title: Trial eligibility in advanced hepatocellular carcinoma: does it support clinical practice in underrepresented subgroups?

Reviewer's code: 03252805

Position: Peer Reviewer

Academic degree: MD

Professional title: Lecturer

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Argentina

Manuscript submission date: 2021-03-17

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-04-19 19:46

Reviewer performed review: 2021-04-22 19:33

Review time: 2 Days and 23 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 checked="" type="checkbox"/> Accept (General priority) <input 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 statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript raised and well discussed the need for representing more subgroups based on clinical practice