PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 75091

Title: Combination Approaches in Hepatocellular Carcinoma: How Systemic Treatment Can Benefit Candidates to Locoregional Modalities

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05199120

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Chief Physician

Reviewer’s Country/Territory: China

Author’s Country/Territory: Brazil

Manuscript submission date: 2022-01-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-24 09:05

Reviewer performed review: 2022-02-02 08:30

Review time: 8 Days and 23 Hours

<table>
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<tr>
<th>Scientific quality</th>
<th>Grade A: Excellent</th>
<th>Grade B: Very good</th>
<th>Grade C: Good</th>
<th>Grade D: Fair</th>
<th>Grade E: Do not publish</th>
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<tbody>
<tr>
<td>Language quality</td>
<td>Grade A: Priority publishing</td>
<td>Grade B: Minor language polishing</td>
<td>Grade C: A great deal of language polishing</td>
<td>Grade D: Rejection</td>
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<tr>
<td>Conclusion</td>
<td>Accept (High priority)</td>
<td>Accept (General priority)</td>
<td>Minor revision</td>
<td>Major revision</td>
<td>Rejection</td>
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<tr>
<td>Re-review</td>
<td>Yes</td>
<td>No</td>
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SPECIFIC COMMENTS TO AUTHORS
Emerging data indicate that locoregional treatments may induce tumor microenvironment changes, such as hyperexpression of growth factors, release of tumor antigens, infiltration of cytotoxic lymphocytes and modulation of adaptative and innate immune response. These events show that the use of systemic agents in combination with local therapy is very important. This review describes the current landscape of systemic and local treatments for HCC, and provide evidences to support combination approaches and future perspectives.
Name of journal: World Journal of Gastroenterology

Manuscript NO: 75091

Title: Combination Approaches in Hepatocellular Carcinoma: How Systemic Treatment Can Benefit Candidates to Locoregional Modalities

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05478444

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Associate Professor

Reviewer’s Country/Territory: Saudi Arabia

Author’s Country/Territory: Brazil

Manuscript submission date: 2022-01-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-12 07:12

Reviewer performed review: 2022-02-13 19:26

Review time: 1 Day and 12 Hours

Scientific quality

[ Y ] Grade A: Excellent
[ ] Grade B: Very good
[ ] Grade C: Good
[ ] Grade D: Fair
[ ] Grade E: Do not publish

Language quality

[ ] Grade A: Priority publishing
[ Y ] Grade B: Minor language polishing
[ ] Grade C: A great deal of language polishing
[ ] Grade D: Rejection

Conclusion

[ Y ] Accept (High priority)
[ ] Accept (General priority)
[ ] Minor revision
[ ] Major revision
[ ] Rejection

Re-review

[ ] Yes
[ Y ] No
SPECIFIC COMMENTS TO AUTHORS

The submitted mini-review: combination approaches in hepatocellular carcinoma: how systemic treatment can benefit candidates to locoregional modalities, presents an interesting look into the available combinatory therapeutic approaches for HCC vs monotherapies like VEGFR-drugs. The following few points are raised:

- Include a section in this review showing all important abbreviations.
- There are number of paragraphs or sentences that need to be connected.
- In the following paragraph: (Combination of ablative and systemic treatment: rationale and current evidence): Give more examples for the novel markers in: (Novel markers such as genetic signatures, circulating microRNA, and circulating tumor cells have also been shown to predict the risk of recurrence).
- Page 13: Guidelines recommend that patients patients who present progression with infiltrative.
- Give example of score(s) in page 13: (The decision to declare TACE failure and switch to systemic treatment is heterogenous in different parts of the world and many scores has been proposed to help in this decision, although some of them still require further validation).
- Page 14: rewrite the following: (It has been demonstrated an increased intratumoral microvessel density and VEGF expression in residual surviving cancerous tissue after TACE).
- Table 1: briefly describe and comment on the RECIST % of the different studies.
- Figure 1: The figure is blurred, make it clearer.
- Figure 2: define the first part of the figure on the left (hepatocells, ...)
Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75091

Title: Combination Approaches in Hepatocellular Carcinoma: How Systemic Treatment Can Benefit Candidates to Locoregional Modalities

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05392001

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: Brazil

Manuscript submission date: 2022-01-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-10 01:03

Reviewer performed review: 2022-02-21 03:06

Review time: 11 Days and 2 Hours

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Hepatocellular carcinoma (HCC) is the fourth cause of cancer-related mortality worldwide, and a wide range of treatment options for HCC are selected based on some clinical standards. Here the authors summarized the current landscape of systemic and locoregional treatments for HCC and showed evidence to support combination approaches and future perspectives. 1, All the figures in this manuscript are too obscure to read. 2, The conclusion part need to polish, to highlight the future of this field and give more suggestions and predictions. 3, Some mistakes in this manuscript need to be improved, i.e. “after tumor ablation and the use immunotherapy is encouraging.”, additional “the” need to remove.