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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 66988

Title: Neoadjuvant treatment strategies for hepatocellular carcinoma

Reviewer's code: 05060622
Position: Editorial Board
Academic degree: MD
Professional title: Associate Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2021-04-19
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-04-20 17:06
Reviewer performed review: 2021-04-29 02:14
Review time: 8 Days and 9 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The authors write a review on the neoadjuvant therapy in HCC. This topic is important and review on this topic is worthy. However, there are severe organizational issues with the manuscript. At several instances, there is a lack of in depth discussion and the authors just give passing references. Specific comments:- 1. Abstract: "Neoadjuvant therapy plays a key role in preventing tumor progression and even downstaging solid tumors"-it is not clear whether authors use it as a general statement or in context of HCC. If in context of HCC, "solid tumors" should be removed. Please remove "clinical" from the last line. 2. WHAT IS NEOADJUVANT THERAPY FOR HCC? The authors highlight three scenarios: bridging, downstaging, and conversion. As these form the basis for further discussion of the paper, these should be clearly discussed, preferably as separate paragraphs. Moreover, in the figure 1, a fourth heading is also added (reduce recurrence-please correct spelling of recurrence in the figure). This, as well as, the description later in the paragraph "Finally, approximately 40% of patients are eligible for radical treatment with an overall survival rate of 70%[26]. Metastasis and new lesions are common types of recurrence[27]. Neoadjuvant therapy plays a certain role in preventing recurrence after radical treatment [28]" causes confusion to the readers. If the authors want to discuss this indication of neoadjuvant, it should be clearly stated with the rest of the indications in the beginning of the paragraph. 3. EFFECT OF NEOADJUVANT THERAPY FOR HCC Why this title, what do you mean by effect. To me the description is more of a repetition or continuation of the above. Moreover, there is a lot of confusion. Can you please improve the organization of contents? In the first paragraph under this section, authors use the term "unobservable adverse effects"-what does this mean?. "Recent studies have shown that the prognosis of patients receiving hepatectomy after successful conversion is comparable to that of patients receiving initial resection"-can you please add more details as it is unclear. 4. PATIENT

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SELECTION AND EFFICACY EVALUATION It should be clarified further whether 20% cut-off for PVE also holds true in the setting of cirrhosis (which is not correct, it is 30%) "The modified Response Evaluation Criteria in Solid Tumors (mRECIST) was performed to evaluate the efficacy of patients receiving neoadjuvant treatment by CT or MRI in most cases. Efficacy evaluation only considers viable tumors"-do you suggest use of other criteria? 5. HOW TO IMPLEMENT NEOADJUVANT THERAPY IN HCC? "Compared with conventional TACE, drug-eluting bead transarterial chemoembolization (DEB-TACE) not only seems to be more capable of inducing tumor necrosis but also reduces the systemic blood concentration and expands the application of TACE"-what do you mean by expand? "Approximately 73-78% of patients within the UCSF criteria achieved successful downstaging, and 40% of them received LT after DEB-TACE[90,95]; the disease control rate was 75-94%"-are there any studies comparing cTACE and DEB-TACE for this indication? "This reminds us that we should not be too optimistic about the efficacy and safety of TACE"-a very vague statement-not suitable for this review PVE: Again please clarify whether 20% FLR cutoff hold true for cirrhosis. What do you mean by reversible PVE. "Overall, PVE is a conversion therapy worth trying" is very vague and not suitable for this review. Radiation therapy and radiofrequency ablation : why combine RFA and radiation therapy. The authors just mention 2-3 lines about RFA and then follow it will radiation therapy. Sorafenib: the authors first write "Sorafenib is also effective in conversion therapy of advanced HCC and even ruptured HCC" and then "However, due to the relatively low response rate of sorafenib in HCC, the application of neoadjuvant therapy is limited[164]. To date, there have been few reports of successful conversion after receiving sorafenib[165-167]."

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Manuscript NO: 66988

Title: Neoadjuvant treatment strategies for hepatocellular carcinoma

Reviewer's code: 03501077

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] 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
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SPECIFIC COMMENTS TO AUTHORS

The paper is well written and the theme is clinically relevant. However, some sentences have to be clarified. "Viral hepatitis is the main risk factor for HCC in East Asia and other regions". The sentence is too vague. Wich regions? "]. Patients within the Milan criteria who have a suitable donor liver at an early stage should undergo LT as soon as possible." This sentence is obvious. "Even patients who have failed downstaging can benefit from neoadjuvant therapy." Wich benefit? "... extrahepatic metastasis and major vascular invasion are absolute contraindications to downstaging treatment[." So, how do you treat these patients?