

1. Reviewer #1: *"Viral hepatitis is the main risk factor for HCC in East Asia and other regions". The sentence is too vague. Which regions?*

Answer: We identified areas where hepatitis B is a major cause of HCC, east Asia and Africa;

2. Reviewer #1: *"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.*

Answer: According to the comments of reviewer 2, we deleted this expression when integrating the second and third parts of previous manuscript;

3. Reviewer #1: *"Even patients who have failed downstaging can benefit from neoadjuvant therapy." Which benefit? "*

Answer: The benefit here means that HCC patients with neoadjuvant therapy could achieve superior prognosis than those without neoadjuvant therapy, although the tumor stage is not declined. We also supplemented the data in the literature to support this claim;

4. Reviewer #1: *"... extrahepatic metastasis and major vascular invasion are absolute contraindications to downstaging treatment [." So, how do you treat these patients?*

Answer: We adjusted the description here: extrahepatic metastasis and major vascular invasion are contraindications to downstaging treatment. Such patients are difficult to achieve tumor downstage due to advanced HCC, so they are not suitable for down-stage treatment in order to receive radical surgery;

5. Reviewer #2: 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.*

Answer: We revised the abstract according to the comments of reviewer 2;

6. Reviewer #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.*

Answer: We adjusted the paragraph layout to describe the four purposes of neoadjuvant therapy in separate paragraphs, explaining the purpose and therapeutic effect of neoadjuvant therapy;

7. Reviewer #2: *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?

Answer: We integrated the second part (WHAT IS NEOADJUVANT THERAPY FOR HCC?) and third part (EFFECT OF NEOADJUVANT THERAPY FOR HCC) of the previous manuscript together, and respectively elaborated on the four major classifications of neoadjuvant therapy in HCC;

8. Reviewer #2: *In the first paragraph under this section, authors use the term "unobservable adverse effects"-what does this mean?*

Answer: We deleted such expression after reviewing related literature;

9. Reviewer #2: *"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.*

Answer: We supplemented the data in literature to strengthen the credibility;

10. Reviewer #2: *PATIENT 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%).*

Answer: We corrected the cut-off value of PVE in the manuscript, and reversible PVE was repeated temporary embolization which was performed in rat model;

11. Reviewer #2: *"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?*

Answer: We added relevant content on the evaluation of the efficacy of neoadjuvant therapy in HCC, and compared the pros and cons of WHO criteria, RECIST criteria, EASL criteria, RECIST1.1 criteria, mRECIST criteria and iRECIST criteria;

12. Reviewer #2: *"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?;*

Answer: There is not enough evidence to support that DEB-TACE is superior to conventional TACE in terms of treatment effect and complications in HCC patients according to clinical research and related meta-analysis;

13. Reviewer #2: *"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;*

Answer: We have deleted this expression in the revised manuscript.

14. Reviewer #2: *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?*

Answer: We have deleted "expand" in this statement;

15. Reviewer #2: *What do you mean by reversible PVE. "Overall, PVE is a conversion therapy worth trying" is very vague and not suitable for this review.*

Answer: Reversible PVE indicates repeated temporary PVE performed on animal models, and *"Overall, PVE is a conversion therapy worth trying"* has been deleted;

16. Reviewer #2: *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.*

Answer: We expanded and discussed the content of radiotherapy and radiofrequency ablation separately;

17. Reviewer #2: *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]."*

Answer: Sorafenib is indeed effective in advanced HCC, but the tumor response rate is relatively low, so there have been few reports of successful conversion after receiving sorafenib;

Finally, we adjusted some of the statements in the manuscript to make it more scientific. The revised part was underlined in the manuscript.