

Thank you for your precious comments. It is very helpful to improve our article. And thank World Journal of Gastroenterology gives us the opportunity to revise our research. According to your suggestions, we have revised it. Hopefully it can reach your requirement.

**Reviewers' comments:**

Reviewer #1: 1 Title. OK 2 Abstract.OK 3 Key words. YES 4 Background. YES 5 Methods. In order to evaluate the data obtained in the HAIC+Lenvatinib combination correctly, the data to be obtained will be much more meaningful if they are compared with the data of the patient group who received only HAIC treatment (as a control group). 6 Results. In order to evaluate the data obtained in the HAIC+Lenvatinib combination correctly, the data to be obtained will be much more meaningful if they are compared with the data of the patient group who received only HAIC treatment (as a control group). 7 Discussion. In the discussion section, it was written that studies with Sorafenib also reported narrowing in tumor-related arterial diameters. It is not enough to just write this as a discussion. In order to evaluate the data obtained in the HAIC+Lenvatinib combination correctly, the data to be obtained will be much more meaningful if they are compared with the data of the patient group who received only HAIC treatment (as a control group). 8 Illustrations and tables. 9 Biostatistics. OK 10 Units. YES 11 References. OK 12 Quality of manuscript organization and presentation. Well written and documented, but needs more data for HAIC and discussion 13 Research methods and reporting. YES 14 Ethics statements. OK:

**Response to Reviewer #1.**

Methods/Results/Discussion. In order to evaluate the data obtained in the HAIC+Lenvatinib combination correctly, the data to be obtained will be much more

meaningful if they are compared with the data of the patient group who received only HAIC treatment (as a control group).

**We thank the reviewer for these important comments. But we are very sorry that we could not provide the data of the patient group who received only HAIC treatment. The ORRs of HAIC monotherapy were low, only 17.6% reported in Ritesh et al study and 24.0% in Song et al study(1, 2). The HAIC monotherapy lacks sufficient evidence as a standard treatment for unresectable HCC. Thus, HAIC was seldom used alone for HCC treatment in our center.**

Discussion. In the discussion section, it was written that studies with Sorafenib also reported narrowing in tumor-related arterial diameters. It is not enough to just write this as a discussion.

**We agree with you. We have made some changes in the paper according to your opinion.**

**Paragraph 2 of DISCUSSION. Hepatic arteries were demonstrated to thin markedly following TKI treatment, and Chen L et al attributed these morphological changes to the anti-angiogenic effect of targeted drugs.**

Reviewer #2: This is a very interesting paper providing insights into the challenging management of unresectable HCC. Could the authors discuss the following: 1) Could the authors compare their approach to other ones including the use of other immune inhibitors or combination of them (ie HIMALAYAS pilot study) 2) Also could the author discuss the possibility of downstaging with this combination

**Response to Reviewer #2.**

1) Could the authors compare their approach to other ones including the use of

other immune inhibitors or combination of them (ie HIMALAYAS pilot study)

**We thank the reviewer for the important comment. The latest research shows that immunotherapy can promote the normalization of tumor blood vessels, which can theoretically enhance the effect of the HAIC+lenvatinib combination. However, we have not used immunotherapy much in the past. Therefore, in this retrospective study, we do not have enough data for relevant comparison. However, according to your opinion, we will carry out further research and discussion in the next study.**

2) Also, could the author discuss the possibility of downstaging with this combination.

**We agree with you. We have made some changes in our manuscript.**

Efficacy, RESULTS. Eight patients received downstaging therapy within 1 year after treatment, of which 6 patients underwent hepatectomy and the other 2 patients underwent radiofrequency ablation.

Paragraph 3 of DISCUSSION. In this study, the ORR reached 68.7%, 66.1%, and 42.9% at 1, 3, and 6 months and conversion therapy was achieved in 8 patients, which further verified the effectiveness of the combination therapy.

## References:

1. Rathore R, Safran H, Soares G, Dubel G, McNulty B, Ahn S, et al. Phase I study of hepatic arterial infusion of oxaliplatin in advanced hepatocellular cancer: a brown university oncology group study. *Am J Clin Oncol*. [Clinical Trial, Phase I; Journal Article; Research Support, Non-U.S. Gov't]. 2010 2010-02-01;33(1):43-6.
2. Song DS, Song MJ, Bae SH, Chung WJ, Jang JY, Kim YS, et al. A comparative study between sorafenib and hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma with portal vein tumor thrombosis. *J GASTROENTEROL*. [Comparative Study; Journal Article; Multicenter Study; Research Support, Non-U.S. Gov't]. 2015 2015-04-01;50(4):445-54.