1. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Reply:

We thank the reviewer for this important suggestion. We have modified the manuscript title as per the guidelines in the revised manuscript.

2. Reviewer #1:

1) Eligible patients: the authors should specify whether enrolled patients had previously received other HCC treatment such as radiofrequency ablation(s), TACE (one or more than one), surgical resection.

Reply:

Thanks you for your critical comments. The enrolled patients did not receiving radiofrequency ablation, TACE, as well as other locoregional treatments four weeks before their admission. We have already made corresponding modifications in the manuscript and highlighted it. At the same time, additional supporting data have been supplemented in Table 1.

2) TACE procedure: could the authors describe how many HCC nodules were treated for any patient? this is a crucial point since an extensive TACE could produce liver function deterioration. Moreover, the authors should recall and discuss a recent study demonstrating a significant correlation between post-procedure transient hypertransaminasemia and objective response obatained with selective TACE, as recently demonstrated (TRANS-TACE: Prognostic Role of the Transient Hypertransaminasemia after Conventional Chemoembolization for Hepatocellular Carcinoma. J Pers Med. 2021 Oct 17;11(10):1041. doi: 10.3390/jpm11101041.)

Reply:

We thank the reviewer again for suggesting this important point. We have included this information in the revised manuscript and highlighted it.

1. Since the whole cohort of the patients had tumor volumes ⩽50% of the liver volume. They were considered eligible for the conventional TACE treatment, hence, the entire intrahepatic

tumor burden was treated by cTACE. None incidences of severe adverse events (SAE) of liver failure were reported in this study.

2. Importantly, a recent study has revealed that transient transaminase elevation (e.g., 52% in ALT; or 46% in AST) after TACE was associated with objective responses [32], which can guide clinical practice. It means that patients with severe liver injury may have limited efficacy from TACE, maybe the severe liver injuries induce liver function deterioration which can hinder the administration of systemic drugs. We have included this information in the Discussion and highlighted it. Also, additional supporting data have been supplemented in Table 4 in the revised manuscript.

3)The last point worth mentioning, is the recent advance in the combined treatment approach of HCC. In this regard, most of current and ongoing clinical trial are based on a TKI plus immune checkpoint inhibitors as recently well-described and summarized (TKIs in combination with immunotherapy for hepatocellular carcinoma. Expert Rev Anticancer Ther. 2023 Mar;23(3):279-291. doi: 10.1080/14737140.2023.2181162). The authors should discuss and compare their results with those of TKI/ICI combination treatments as reported in this recent review (TKIs in combination with immunotherapy for hepatocellular carcinoma. Expert Rev Anticancer Ther. 2023 Mar;23(3):279-291. doi: 10.1080/14737140.2023.2181162).

Reply:

Thanks for your valuable suggestions. The suggested reference has been added.

In the era of combination drug therapies, TKIs combined with ICIs, such as, Lenvatinib combined with Pembrolizumab or Nivolumab, Cabozantinib combined with Nivolumab/Atezolizumab, have been proven to offer higher efficacy and longer OS in HCC patients [29]. The addition of TACE further improves the response of this combination (TKI plus ICI) therapy for advanced-stage HCC subjects [21,22,30]. We have made the necessary changes and highlighted them in the revised manuscript.