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Editors-in-Chief

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Dear Drs Hu, Kang, and Pyrsopoulos,

Thank you for the opportunity to submit a revised version of our manuscript "Successful hepatic resection for recurrent hepatocellular carcinoma after lenvatinib treatment: case report" (Manuscript No.: 58594), for possible publication as a Case Report in *World Journal of Hepatology.* We greatly appreciate the reviewers' incisive comments that have helped us to significantly improve the manuscript. Below are our point-by-point responses to the reviewers' comments, with descriptions of the changes made to the manuscript. In the revised manuscript, **red** text indicates portions revised according to the comments of Reviewer #1 and **blue** text indicates portions revised according to the comments of Reviewer #2.

We hope that our paper is now suitable for publication in *World Journal of Hepatology*.

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We appreciate your kind consideration of our manuscript, and look forward to hearing from you at your earliest convenience.

Yours sincerely,

Hideki Yokoo, MD, PhD

Response to Reviewer #1

Major concerns

1) In “Multidisciplinary Expert Consultation” section, the authors decided to administer lenvatinib to suppress the rapidly increasing intrahepatic lesion and before surgery. It is desirable to present a full discussion of the reasons for not choosing surgical resection without prior lenvatinib

Response: The reason for not choosing surgical resection without prior lenvatinib was that the site of recurrence was rapidly increasing, and it was thought that new lesions might appear in other parts of the liver immediately after surgical resection. We have added this information to the “Multidisciplinary Expert Consultation” section (page 7, lines 181–184).

2) In order to achieve shrinkage of the intrahepatic main tumor, transcatheter therapy, such as B-TACE instead of Lenvatinib, is an option. The reasons for choosing prior treatment with lenvatinib should be fully described.

Response: The reason for choosing lenvatinib was that in addition to the intrahepatic recurrence, there was a sternal metastasis. Therefore, we considered that systemic therapy would be better than transcatheter therapy, such as B-TACE. We have added this information to the “Multidisciplinary Expert Consultation” section (page 7, lines 179–181).

3) In “Final Diagnosis” section, the authors evaluate therapeutic response to lenvatinib by CT imaging after 1 month of lenvatinib administration. If

lenvatinib had been so effective, there would have been an option to continue further treatment. It is advisable to fully describe the reasons for the decision to perform surgery at this time.

Response: First, long-term administration of lenvatinib may result in decreased liver function such as decreased albumin, which can make surgery impossible. Second, early surgery was selected because it was unknown whether lenvatinib would result in CR and it was better to aim for complete removal of the tumor by surgery. We have added this information to the "Treatment" section (page 8, lines 199–204).

4) Has there been a recurrence of HCC in the postoperative period to date, and how long has lenvatinib been administered postoperatively?

Response: At 1 month after the end of radiotherapy, there was a small intrahepatic recurrence, and lenvatinib was immediately administered. PR was obtained, and the patient has remained alive on administration for 1 year after the second hepatectomy. This description has been amended in the "Outcome and Follow-up" section (page 8, lines 210–213).

Minor concerns

1) In "Introduction" section, "Hepatic artery embolization and chemotherapy" should be changed to "Transarterial chemoembolization (TACE)".

Response: We appreciate this comment. In accordance with the reviewer's comment, we have changed "Hepatic artery embolization and chemotherapy" to "Transarterial

chemoembolization (TACE)" in the Introduction section (page 5, line 105).

2) In "Laboratory examinations" section, it would be better to describe Child-Pugh score/classification and ALBI score/mALBI grade. Was mALBI grade 2a or 2b?

Response: In the "Laboratory Examinations" section, we have revised the indicated sentence as follows: "Child–Pugh score/classification was 5/A and the albumin-bilirubin (ALBI) score/modified ALBI grade was −2.19/2b." (Page 6, line 157 to page 7, line 159

3) In "Imaging examinations" section, the authors described that the mass rapidly increased in 5 months. Please show the CT image 5 months before.

Response: A CT image at 5 months before the second operation was not taken. However, MRI images at 5 months before the second operation have been provided in Figure 1 (A: T1 image; B: T2 image). There was no evidence of the recurrent tumor on the MRI images (page 7, lines 166–168).

4) In "Imaging examinations" section, the authors described that elevated FDG uptake was shown in the sternum. Was the main tumor also showed elevated uptake of FDG? Please show the PET image.

Response: A PET image of the main tumor has been provided in Figure 3B. The main tumor also showed slightly elevated uptake of FDG (page 7, line 169).

5) In “Multidisciplinary Expert Consultation” section, the authors described lenvatinib was administered at a dose of 8 mg, not 12 mg. Was the patient weigh less than 60 kg?

Response: The patient’s weight was 59 kg. We have added this information to the “Physical Examination upon Admission” section (page 6, line 150) and the “Multidisciplinary Expert Consultation” section (page 7, lines 176–177).

Response to Reviewer #2

1.) lenvatinib has emerged in the first-line setting after a positive phase 3 study, Although conversion therapy for HCC has not yet been established, lenvatinib is expected to be a possible candidate agent. In this case, lenvatinib induced a partial response (PR) for rapid growth of recurrent HCC with bone metastases, and conversion to surgery was successfully achieved for the purpose of controlling the intrahepatic lesion for the first time. Provides a new treatment perspective for recurrent HCC.

Response: We appreciate these comments. The following text was added to the Discussion section: “lenvatinib is expected to be a possible candidate agent and provides a new treatment perspective for recurrent HCC.” (Page 9, lines 224–225)

2.) 2.Sorafenib has been the first-line treatment in this setting for almost a decade. Why not choose Sorafenib for treatment? Have you tried before?

Response: Sorafenib did not show a tumor shrinkage effect in the SHARP and Asian

Pacific studies. Meanwhile, lenvatinib was shown to be noninferior to sorafenib for unresectable hepatocellular carcinoma, and tumor shrinkage was observed in ~40% of cases. For this reason, lenvatinib was selected because of the high probability of conversion due to the tumor shrinkage effect (page 5, lines 118–122).