ANSWERS for REVIEWER COMMENTS

February 10, 2013

Dear Editor,

Please find enclosed the edited manuscript in MS-Word 2010 format (file name: 1767_Text_R1.docx).

Title: Active treatments are rational approach for hepatocellular carcinoma in elderly patients. Intervention in the HCC elderlies

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1. **Format has been updated.**

2. **Revision has been made according to the suggestions of the reviewers as follows.**

R1-Q1: There are limitations that this study is performed in single institution and the number of patients is limited.

R1-A1: Yes, I agree that our study has a limitation in regard to the number of institution and patients. A description about the limitation was added in the revised version (P16, L16).

R1-Q2: In table 1, the number of patients who evaluated HBsAg (-/+/ND) was 818, although the total number of enrolled patients was 918.

R1-A2: Thank for your careful reading of my manuscript. That is a simple typo. It should be "196" instead of "96" and was corrected in the revised version.

R1-Q3: How did you classify the patient managed with multimodality approach?

R1-A3: As I mentioned in the material and methods section, a case was classified into a group according to the applied treatment with the highest regional control capability when pleural treatments were added as an adjunct (P7, L14).

R2-Q1: The authors used percent life expectancy to conclude that %LE can be a more useful indicator to compare survival benefit between older age group and younger age group with HCC. It is uncertain to get this conclusion since that, as comparing with younger non-HCC cohort, the expected residual life length is far less in older age patients who might have serious comorbidities and in aging; naturally, %LE could be higher significantly in older patients. It would be assumed inappropriately that older patients with HCC (or other serious systemic diseases) had better survival benefit.

R2-A1: I understand the reviewer's concern. If it is the case, the survival benefit should be better in the order of aging when %LE is simply compared among different age groups using Kaplan-Meier

method. As you can see in the figure 2b, however, the Kaplan-Meier fractions were similar among the different age groups except for the youngest, and the distribution quite resembles the fraction of survival days as shown in the figure 1b. Furthermore, the beneficial order is similar between Kaplan-Meier fractions and COX regression suggesting that %LE is not simply distributed in the order of aging. As I described in the first paragraph of the discussion section, a poor prognosis in the youngest age is logically consistent with our experience. Because our conclusion was drawn based on the data from a single institution with a limited number of patients, a description about the limitation of our study was added in the revised version (P16, L16).

R2-Q2: The authors concluded that a therapeutic approach for HCC should not be restricted due to patient age. However, there is no enough data to clarify this conclusion.

R2-A2: I agree that our conclusions should be further tested and confirmed in a multicenter study using a larger cohort to become concrete evidence. In the revised version, the expression was modified to be less forceful (P3, L14).

R2-Q3: The writing in part of the manuscript is redundant. There are repetitive in table footnotes and figure legends. It would be much simple to make labels on figures directly instead of writing redundant figure legends.

R2-A3: I do not have any intension to keep the style in the original version. Rather, I would like to follow the Journal policy. Please specifically indicate the redundant part and a preferable style of figures and figure legends according to your Journal policy.

R2-Q4: The case presentation did not offer further additional information, so it could be omitted.

R2-A4: I am sure that many physicians hesitate to implement a reservoir and perform chemotherapy to a patient at age of 85 years with a comorbidity of diabetes mellitus requiring insulin shots. I believe a presentation of actual case significantly emphasizes our conclusion that an invasive treatment can apply safely and effectively even for the elderly patients.

3. References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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