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Prof. Clara Balsano and Wan-Long Chung

Editor-in-Chief, *World Journal of Hepatology*

November 12, 2016

Dear Professor Clara Balsano, Professor Wan-Long Chung and reviewers

On September 29th, we received your letter with the reviewer's comments. Thank you very much for your review of our manuscript entitled "Role of surgical resection for non-colorectal non-neuroendocrine liver metastasis (29880)."

Enclosed please find our replies to the comments made by the reviewers 00537002, 02861333, and 00503563 along with the new version of our manuscript, which has been revised based on the reviewers' comments, and has undergone appropriate English proofreading. All revisions and additions to the text are indicated in BOLD RED in the revised manuscript. We believe that the presentation of our findings in the manuscript has been markedly improved.

We appreciate your kindness and thank you again for your time and effort in re-reviewing our manuscript.

Sincerely yours,

Nobuyuki Takemura, MD

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Our point-by-point replies to all comments by the associate editor and the reviewers 00537002, 02861333 and 00503563 are as follows.

Reply to the one comment made by Reviewer 00537002

Thank you for your kind comment regarding this manuscript, suggesting it is acceptable for this journal. Your comment was encouraging to us.

1. *Nice paper. Well conducted study. Clear aims, clear final message*

Replies to the one comment made by Reviewer 02861333

Thank you for your appreciation of this manuscript. Our reply and revisions are as follows.

1. *What about the surgical or combined therapy results for liver metastasis from breast cancer or genitourinary tumors with different genetic mutations?*

As a representative example, *BRCA* gene mutations are well-known risk factors for breast and ovarian cancer. It is important for the prevention of these diseases for affected women to undergo prophylactic bilateral salpingo-oophorectomy and risk-reducing mastectomy; however, *BRCA* mutation status is not more important than ER/PGR and HER2 statuses when selecting treatments for patients with breast cancer. Genetic mutations have not had been studied sufficiently to affect clinical practice yet except for HER2. In response to the reviewer's comment, we added the following comment about HER2 as one of the genetic mutations.

New (page 11, lines 8-9)

Some prognostic factors of liver metastases from breast cancer are unique and different from other NCNNLMs, which could indicate that the presence of hormone receptors **and HER2 overexpression requires the use of chemotherapy and/or hormone therapy and** influences patient survival.

Replies to the 2 comments made by Reviewer 00503563

Thank you for your appropriate comments and recommendations. Our replies and revisions are as follows.

1. *The authors should discuss about the future perspective of surgical management in non-colorectal non-neuroendocrine liver metastasis based on results obtained from review in Discussion section.*

We added the following sentences about the further perspectives of surgical management of NCNNLM in the last section.

New (page 14, lines 19-22)

Indications of hepatectomy for NCNNLM change according to the development of chemotherapy regimens. Strong and highly effective chemotherapy regimens might either expand the indications for hepatectomy or replace hepatectomy in this field.

2. *In Table, mortality/morbidity should be deleted.*

In response to your comments, the information about mortality/morbidity in all of the tables were deleted.

English proofreading has been performed again by a native English speaker.

Finally, we appreciate your kindness and thank you again for your time and effort in re-reviewing our manuscript. We look forward to receiving a favorable reply from you.

Sincerely

Nobuyuki Takemura, MD