

Dear Prof. Patel,

Editor-in-Chief, World Journal of Clinical Oncology

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Dear Editor,

Thank you very much for review of the manuscript (Manuscript No: 48929) that we sent on May 15, 2019. We thank editorial office and two reviewers for providing constructive comments regarding the improvement of the original manuscript.

We believe have resulted in an improved revised manuscript, which you will find uploaded alongside this document. All changes have been made in response to the reviewers' suggestion, and itemized response to the individual reviewer's comments are also attached.

Thank you once again for your consideration of our paper.

Sincerely yours,

Chiaki Inagaki M.D.

on behalf of the authors

e-mail: cinagaki@cfs.med.osaka-u.ac.jp

Reviewer #1:

Minor comments;

The authors need to cite - a) the largest and most recent study of ERBB2 in gallbladder cancer: ERBB2 and KRAS alterations mediate response to EGFR inhibitors in early stage gallbladder cancer. Iyer P, Shrikhande SV, Ranjan M, Joshi A, Gardi N, Prasad R, Dharavath B, Thorat R, Salunkhe S, Sahoo B, Chandrani P, Kore H, Mohanty B, Chaudhari V, Choughule A, Kawle D, Chaudhari P, Ingle A, Banavali S, Gera P, Ramadwar MR, Prabhash K, Barreto SG, Dutt S, Dutt A. Int J Cancer. 2019 Apr

15;144(8):2008-2019. b) the most comprehensive update on Gallbladder Carcinogenesis published to date: A genetic model for gallbladder carcinogenesis and its dissemination. Barreto SG, Dutt A, Chaudhary A. Ann Oncol. 2014 Jun;25(6):1086-97.

A. We appreciate helpful suggestion of Reviewer 1. As you indicated, we added two literature in the reference(p.14, l.1).

Reviewer #2:

Minor comments;

Q1. Mutation of TP53 at metastatic lesion should also be described.

A1. Thank you for your comment. You may find the reason that we did not mentioned TP53 mutation at the metastatic site in the manuscript (p.11, l.6-8). *TP53* was not included in the gene list of NGS panel used for an analysis of the metastases.

Q2. The management for AE of lapatinib and capecitabine for GBC patients should be discussed.

A2. We appreciate helpful suggestion of Reviewer 2. As indicated, we have added the sentence (p.12, l.11-12).

Q3. Authors should discuss about the effect of prior standard therapy such as GC or S1 should be considered

A3. As the patient's best responses to both the 1st line and 2nd line chemotherapy were progressed disease, so we originally wrote "her disease did not respond to these agents". To make this point more clearly, we have revised the text (p.11, l.16).