

## Format for ANSWERING REVIEWERS



August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6726-review.doc).

**Title: Molecular targeting to treat gastric cancer**

**Author:** Keishiro Aoyagi, Kikuo Kouhiji, Junya Kizaki, Taro Isobe, Kousuke Hashimoto, Kazuo Shirouzu

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 6726

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 reviewer

(1) 00004520

Thank you for your useful comments.

I reply for your comments as bellow.

- 1) I added the behavior of the potential molecular targets in gastric cancer to Introduction.  
I described about EGFR including HER2, VEGF/VEGFR, mTOR, and its molecular targeting drug in Introduction of revised article.
- 2) I added three figures, Fig. 1:HER2 signaling pathway; Fig. 2:VEGFR signaling pathway; Fig. 3 EGFR signaling pathway in revised article.
- 3) I added the evaluation of the therapeutic potential of each molecular target agent to each paragraph.  
However, I had already described about the therapeutic potential of everolimus and panitumumab in first article.
- 4) I added the another paragraph "Other molecular targeting therapies" in revised article. We shortly described about matuzumab, tivantinib, and new targeting therapy for STAT 3.

(2) 01551804

Thank you for your useful comments.

I reply for your comments as bellow.

Major comment

I described about S-1 plus cisplatin (SP) and trastuzumab end of paragraph 1) in revised article.

Minor comment

I change "ICQ" to "ICH" at Page 6 , line 7 in revised article

3 References and typesetting were corrected

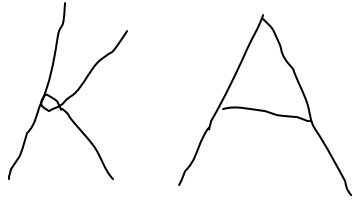
I added followed references in revised article.

39. **Boku N**, Yamamoto S, Fkuda H, Shirao K, Doi T, Sawaki A, et al. Fluorouracil versus combination of irinotecan plus cisplatin versus S-1 in metastatic gastric cancer: a randomized phase 3 study. *Lancet Oncol.* 2009;**10**:1063-9

40. **Koizumi W**, Narahara H, Hara T, Takagane A, Akiya T, Takagi M, et al. S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial. *Lancet Oncol*. 2008;**9**:215-21
41. **Honma Y**, Shimada Y, Takashima A, Iwasa S, Kato K, Hamaguchi T, et al. Efficacy of S-1 plus cisplatin combination chemotherapy in patients with HER2-positive advanced gastric cancer. *Int J Clin Oncol*. 2013  
Published online
- 111**Rao S**, Starling N, Cunningham D, Sumpter K, Gilligan D, Ruhstaller T, et al. Matuzumab plus epirubicin, cisplatin and capecitabine (ECX) compared with epirubicin, cisplatin and capecitabine alone as first-line treatment in patients with advanced oesophago-gastric cancer: a randomized, multicentre open-label phase II study. *Ann Oncol*. 2010;**21**:2213-9
- 112**Trarbach T**, Przyborek M, Schleucher N, Heeger S, Lüpfer C, Vanhoefer U. Phase I study of matuzumab in combination with 5-fluorouracil, leucovorin and cisplatin (PLF) in patients with advanced gastric and esophagogastric adenocarcinomas. *Invest New Drugs*. 2013;**31**:642-52
- 113**Gherardi E**, Birchmeier W, Birchmeier C, Vande Woude G. Targeting MET in cancer: rationale and progress. *Nat Rev Cancer*. 2012;**12**:89-103
- 114**Munshi N**, Jeay S, Li Y, Chen CR, France DS, Ashwell MA, et al. ARQ 197, a novel and selective inhibitor of the human c-Met receptor tyrosine kinase with antitumor activity. *Mol Cancer Ther*. 2010;**9**:1544-53
- 115**Kang YK**, Muro K, Ryu MH, Yasui H, Nishima T, Ryoo BY, et al. A phase II trial of a selective c-Met inhibitor tivantinib (ARQ 197) monotherapy as a second- or third-line therapy in the patients with metastatic gastric cancer. *Invest New Drugs*. 2013;Published online
- 116**Okamoto W**, Okamoto I, Arano T, Yanagihara K, Nishio K, Nakagawa K. Differential roles of STAT3 depending on the mechanism of STAT3 activation in gastric cancer cells. *Br J Cancer*. 2011;**105**:407-412
- 117**Giraud AS**, Manheniott TR, Judd LM. Targeting STAT3 in gastric cancer. *Expert Opin Ther Targets*. 2012;**16**:889-901

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

Sincerely yours,



Keishiro AOYAGI, MD, PhD  
Dept. of Surgery  
Kurume University School of Medicine  
67 Asahi-machi, Kurume  
830-0011 Japan  
Fax: +81-942-34-0709  
E-mail: [keishiro@med.kurume-u.ac.jp](mailto:keishiro@med.kurume-u.ac.jp)