

Format for ANSWERING REVIEWERS



October 29, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6106-Review.doc).

Title: Adjuvant chemotherapy, p53, carcinoembryonic antigen expression and prognosis after D2 gastrectomy for gastric adenocarcinoma

Author: Ming-ming He, Dong-sheng Zhang, Feng Wang, Zhi-qiang Wang, Hui-yan Luo, Chao Ren, Ying Jin, Dong-liang Chen, Rui-hua Xu.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6106

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

1 Format has been updated.

2 According to the suggestions of the editor, for this manuscript submitted by non-native speakers of English, we had sought to make use of a copyediting service provided by professional English language editing company, Jing-Yun Ma Editorial Office: <http://majingyun.baikemy.com>. After the professional English language editing, we believe the language of our manuscript reaches or exceeds Grade A (priority publishing) on the basis of previous Grade B (minor language polishing). We also submitted the EDITORIAL CERTIFICATE.

3 Revision has been made according to the suggestions of the reviewer

For reviewer 1

(1) Thank you so much for your attentive revision, especially for the appropriate references you suggested to include. We have followed your requirements, added the specified references to the discussion in the suitable location.

(2) Thanks again for your serious and earnest review. We revised the "there're" to "there are".

For reviewer 2

(1) Thank you so much for your attentive revision. You concerned the ethical issue. We had made an addition to the previous ethics and stated that "all these patients had their consent about the two forms of treatment and involved in the decision-making of receiving adjuvant chemotherapy or not" in subtitle Patients.

(2) Thank you so much for your attentive revision. You concerned why fluoropyrimidine monotherapy and fluoropyrimidine plus platinum adjuvant regimens yielded better results and suggested us include the possible unique anti-tumor mechanisms of fluoropyrimidine in discussion. We discussed on this point and summarized the genetic mechanism of cellular cytotoxicity to fluoropyrimidine and also the synergism that platinum plus fluoropyrimidine in the 3rd paragraph of discussion.

(3) Thanks again for your serious and earnest review. We revised the topographical use of words, including the "wasn't" to "was not", "they're" to "they're", "there's" to "there is" and so on. We also checked and revised the spelling and grammar in the manuscript as well.

For reviewer 3

(1) Thank you so much for your attentive revision. You concerned the 3-year OS, 3-year DFS of this study was lower than what was reported in CLASSIC study and ACTS-GC study. Your suggestion was appreciated and we had discussed that one point was that we included both R0 and R1 radical gastrectomies while the above three phase 3 trials only focused on R0 radical gastrectomy. Another point was that we included all stage II/III patients according to AJCC stage(7th), while the the CLASSIC study included stage II/III gastric cancers but no T4bN+ or N3b were included, and more evidence for stage IIIB and IIIC patients are warranted. ACTS-GC study showed a survival benefit for stages II and IIIA disease according to AJCC stage(7th), not for IIIB and IIIC patients. The subgroup analysis of patients with R0 gastrectomy was consistent with the results for the entire cohort (OS: 52.27 vs 31.67 mo, $P = 0.000$; DFS: 36.93 vs 26.20 mo, $P = 0.004$; 3-year OS rate: 74.2% vs 55.0%, $P = 0.001$; 3-year DFS rate: 59.7% vs 45.4%, $P = 0.036$) after excluding the R1 subgroup. Furthermore, we focused on patients with R0 gastrectomy excluding T4bN+ or N3b disease (3-year OS rate: 76.1% vs 56.4%, $P = 0.000$; 3-year DFS rate: 61.0% vs 48.2%, $P = 0.006$), for whom survival came nearer to results of the CLASSIC study. Of note, 13.6% patients with T4bN+ or N3b disease were included in our entire population, higher than 6.9% in ACTS-GC study. The subgroup results excluding T4bN+ or N3b disease came nearer to those in ACTS-GC study (3-year OS rate: 82.63% vs 75.2%, 3-year RFS/DFS rate: no subgroup analysis). Please view the relative changes in discussion part of the manuscript.

(2) Thank you so much for your attentive revision. You concerned that in addition to nodal stage and T stage, postoperative complication was a prognostic factor for survival. Your suggestion was appreciated and we agreed it is important for discussing postoperative complication in the analysis of survival. We acknowledge that the limitations of this study are the retrospective setting and no analysis of postoperative complication. Although no vital complications were observed post-operatively, no detail records of postoperative complication were retrospectively analyzed. We found this was a limitation of the available phase 3 clinical trials, too. We wish this issue would be highlighted in the future studies.

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

Sincerely yours,



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