ANSWERING REVIEWERS

September 4th, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4979-review.docx).

Title: Non-platinum-based chemotherapy for treatment of advanced gastric cancer: 5-fluorouracil, taxanes, and irinotecan

Author: Byung Woog Kang, Jong Gwang Kim, Oh-kyoung Kwon, Ho Young Chung, Wansik Yu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4979

The manuscript has been improved according to the suggestions of reviewers:
1 English language of this manuscript has already been edited by a private company. Thus, we enclose the e-mail from that company.

Dear Byung Woog Kang, Please find attached my revised version of your paper.
As always, my revisions can be highlighted/hidden/accepted by clicking on the MS Word Review/Final/Accept options. I have also attached a revised version without highlights.
The total charge is 60,000 won (6 pages, 11 font, double-spaced x 10,000 won) Please pay this amount into the following account: Daegu Bank Account number: 075 08 046983 4 Account name: Hwang David Dae Sung
Please confirm receipt of paper.
Best regards Lorne Hwang

Reviewed by 00001114
This paper seems platinum agents is too toxic to affect the final treatment outcomes hand quality life majority of patients with advance gastric cancer. On the other hand, SPIRITS trial (Lancet Oncol. 2008) showed a survival benefit of S-1 plus cisplatin over S-1 and S-1 plus cisplatin therapy results in the establishment of a standard care for advanced gastric cancer in Japan. Therefore, I feel something different with this review even though I understand that newer agents are considered as a preferred option for first-line chemotherapy in patients with advanced gastric cancer. I have the following comments – I was wondering how the authors evaluate platinum agents play in chemotherapy for patients with advanced gastric cancer. As far as I understand, non-platinum agents was sometimes used alone for chemotherapy in patients with advanced gastric cancer, but platinum agents was usually used as combination with other drugs, not in single agent. Therefore I get the feeling that readers confuse because platinum agents is equally positioned as other cytotoxic agents. **Please explain the position of platinum in chemotherapy for advanced gastric cancer.**

Author's answer
We appreciate deeply the time and consideration that editor and reviewers have given to this manuscript. We agree with many of the reviewer's comments and we now realize that there are some points that we need to explain more clearly. The manuscript has also been enriched by your suggestions.
Reviewer's question touches the very essence of this manuscript, and authors agree with reviewer's opinion. According to reviewer's suggestion, the new paragraph has been added in the main text just after INTRODUCTION section. **(Title: The role of platinum-based chemotherapy in AGC)**

"Platinum-based doublet chemotherapy, typically cisplatin in combination with either infusional 5FU or an oral 5FU, such as S-1 or capecitabine, is current standard practice in many countries[1]. In a randomized

phase III trial (SPIRITS trial)[10], 298 patients with AGC were randomized to S-1 plus cisplatin and S-1 alone. Median progression-free survival (PFS) (6.0 versus 4.0 months) and overall survival (OS) (13.0 versus 11.0 months) were significantly longer in the combination group. Response was also higher with S-1 (54% versus 31%). Based on this trial, S-1 plus cisplatin combination regimen has been established as a standard treatment for AGC in Japan. Two phase III trials have compared the efficacy and safety of cpaecitabine-based and 5FU-based combinations. In Western countries, the REAL-2 trial was a randomized multicenter phase III study comparing capecitabine with 5FU and oxaliplatin with cisplatin in 1003 patients with AGC[11]. Although 30% of patients had an esophageal cancer, results from this study suggest that capecitabine and oxaliplatin are as effective as 5FU and cisplatin, respectively. Another phase III randomized trial (ML17032 trial) evaluated the combination of capecitabine and cisplatin versus the combination of 5FU and cisplatin in patients with AGC[12]. Capecitabine and cisplatin combination was met the primary endpoint of non-inferiority of PFS (5.6 versus 5.0 months). Median OS (10.5 versus 9.3 months) and severity of adverse events were comparable in both groups. Consequently, oral 5FU (capeciatbine or S-1) and platinum-based combination has been widely accepted as one of the first choices for treatment in patients with AGC over the world."

2 Revision has been made according to the suggestions of the reviewer
(1) Postal code added: 702-210
(2) All authors' contribution has been provided according to the suggestion.
(3) In order to help reviewer and readers' better comprehension, we added the core tip.
(4) Heading 2 was changed in italic type throughout the manuscript.
3 Each DOI citation number in references section has been newly provided.

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

Sincerely yours,
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