

**Dear Editors and Reviewers:**

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "**Docetaxel, Cisplatin, and 5-fluorouracil (DCF) Compared with Epirubicin, Cisplatin and 5-fluorouracil (ECF) Regimens for Advanced Gastric Cancer: A Systematic Review and Meta-Analysis**" (Manuscript NO: 43237). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have carefully revised the manuscript according to the reviewers' comments. Revised portions are marked in red in the paper. The main corrections in the paper and the responses to the reviewer's comments are as follows:

**Responses to the editor's request:**

**1. request:** Please update the reference numbers.

**Response:** We have updated all the reference numbers in this article.

**2. request:** Please write the article highlight section according to the guidelines.

**Response:** We have completed this part of the article highlights according to the guidelines.

**3. request:** Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

**Response:** We have updated all the references. We have added PMID and DOI to all the references that can be added. There are few references without PMID and DOI. We provide the first page of the paper as required.

**4. request:** Please provide the figure 1 in a word format. So that we can edit the word in the figures

**Response:** We have provided the word format of figure 1 as required.

## **Responds to the reviewer's comments:**

### **Reviewer #1:**

We would like to thank the reviewer for his recognition of the significance of our study.

**1. Comment:** Line 79: Patients have post-operative recurrence when diagnosed. This does not make any sense. I assume the authors mean that most patients present with advanced disease and who are treated radically, develop recurrence.

**Response:** We are very sorry for our incorrect writing. This sentence does make people misunderstand. Our intention is that many patients are unable to get timely diagnosis and effective treatment due to the lack of obvious symptoms in the early stage, leading to the advanced gastric cancer. Moreover, many patients are likely to relapse even after regular radiotherapy and chemotherapy. We have carefully corrected this mistake throughout the manuscript according to your comment.

**2. Comment:** Figures 5 and 6 contain a large amount of information and therefore the font size is very small. The presentation of this should be improved.

**Response:** In the data analysis, we had found the problem of too small fonts in figures 5 and 6. In print journal, it is hard to obtain the information above for the small size of the font. So, we will submit high-resolution images (which can be downloaded online) in the revision. This will make it easier for the reader to get the data from the images.

Thank you for your careful reading of our manuscript. Special thanks to you for your good comments.

### **Reviewer #2:**

We would like to thank the reviewer for his recognition of the significance of our study.

**1. comment:** The authors showed that the DCF group was significantly better than the ECF group in terms of ORR and DCR. What kind of reason do the authors think for

these results? The authors should mention it in Discussion.

**Response:** Thank you for your valuable advice. These results might be because docetaxel had better efficacy, and the patient's response to this drug was relatively high. Its curative effect is largely related to its mechanism of action. In the discussion section, we add the mechanism of action about docetaxel and epirubicin (Added content: Docetaxel is a taxane compound discovered in the 1990s. It mainly enhances tubulin aggregation and inhibits microtubule depolymerization, leading to the formation of stable non-functional microtubule bundles, thus destroying the mitosis of cancer cells to achieve anti-tumor effect. Compared with paclitaxel, it has stronger activity and broader anti-tumor spectrum. Epirubicin is an antibiotic anti-tumor drug, which belongs to non-specific cell cycle anti-cancer drugs. Its mechanism is to directly insert DNA nucleotide pairs to interfere with the transcription process and prevent the synthesis of RNA and DNA.).

**2. comment:** The authors used seven meta-analysis in this manuscript. However, the doses of anticancer agents were different in each study. Therefore, it seems to be difficult to analyze all together.

**Response:** The comment is very pertinent. Because of the different acceptance of this drug by different manufacturers and clinicians, there are some dose differences in the seven studies we included. Although it may have some impact on our results, the differences don't show any statistical significance, especially in docetaxel and epirubicin. However, it is true that disunity of drug dosage will influence the merging of data between the included studies, which may increase heterogeneity. We have added this limitation in the discussion.

**3. comment:** (Results, Toxicities) Figure4B→Figure6.

**Response:** We are sorry for our careless mistake. We have corrected it in our revised

manuscript.

**4. comment:** The authors found high incidences of neutropenia and febrile neutropenia in the DCF group. How was the reduction or stop of anticancer agents performed?

**Response:** As our results show, DCF showed greater adverse effects on neutropenia and febrile neutropenia. The toxicity profile of DCF is acceptable only with appropriately selected patients and comprehensive toxicity management strategies. It is interesting to note that after appropriate dose reduction, the rate of neutropenia and febrile neutropenia was reduced of cycles with DCF. European and North American guidelines recommend the routine use of primary G-CSF prophylaxis when using chemotherapy regimens associated with a risk of neutropenia and febrile neutropenia. Therefore, we have completed the relevant introductions in the discussion section.

Thank you for your careful reading of our manuscript. Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval. At the same time, we wish we can hear the positive decision/comments from the editors/external reviewers as soon as possible.

Once again, thank you very much for your comments and suggestions.

Thank you and best regards.

Yours sincerely,

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