8 Sep 2018,

Dear Editor and Reviewers,

I would like to thank the editorial office for their consideration of our manuscript to *Word Journal of Gastrointestinal Oncology*. Also I would like to thank the reviewers, for taking their time and giving valuable feedbacks on our manuscript.

I adopted the comments of the reviewers and revised the manuscript accordingly. Please refer to the table below for summarized changes of the manuscript. Also, every changes in revised manuscript are marked in yellow.

Thanks again to the reviewers and editorial office of the *Word Journal of Gastrointestinal Oncology* for kindly reviewing our manuscript. Please contact us if there are any additional requirements.

Sincerely,

Jeong Youp Park, MD, PhD

Comment	Answer
Editor	
Please rearrange this part into a separated one, subtitled as statistical analysis. (page 8)	Thank you for your kind review and comments. We rearranged sentences about study endpoints to "Assessment of treatment efficacy" and "Assessment of adverse events" section. **(Line 1 of each sections, page 8)** **Change subtitle (page 8):** "Study endpoints and statistical methods" → "Statistical analysis" **Line 6-7 of "Statistical analysis" section in the materials and metods (page 8):** P-value <0.05 was considered statistically

	significant. **Figure 2A and 2B were changed to improve the readability**
Reviewer #1 (02537436)	
1) In line 4-5 of results in abstract, line 6 in treatment responses and survival of page 9 and line 2 of page 10, author showed only adjusted data. I think raw data are more significant than adjusted. Please discribe the unadjusted data of PFS and OS firstly.	Thank you for your kind review and comments. P-values showed in comparison of PFS and OS of both groups were calculated with non-adjusted data. They were calculated by log-rank test. Regarding to adjust HRs, because 95% confidence intervals crossed 1.0, both HRs were not significant. However, because HR and p-value were demonstrated in the same parentheses at once, we agree that the p-value could be mistaken as belonging to HR, which was calculated by Cox proportional-hazards model. To solve this problem, we changed result of abstract and main manuscript**.** **Line 5-6 of results in abstract (page 3):** we omitted to mention adjusted HRs. Only survival comparison and its p-value by log-rank test are now described. **Line 4-11 of 'Treatment responses and survivals' section of the result in main manuscript (page 9-10):** we describe survival comparison with p-value by log-rank test first, and then we present adjusted HR with its own p-value by Cox. Additionally, we also deleted HRs and 95% CIs in Figure 2A and Figure 2B, to avoid misunderstandings.
2) In line 2 in treatment characteristics of page 9, author mentioned "treatment durations were statistically similar". I think statistical analysis showed "no	We agree your comment and changed that sentence. **Line 1-2 of 'Treatment characteristics' section of the result (page 9):** "The number of cycles administered and

difference between two groups" but "similar". Please reconsider statistical interpritation.	treatment duration were not different between the two groups". We also found several same misinterpretations, and changed them. **Line 1 of conclusion in abstract (page 3)**: "similar" → "comparable" **Line 7 of 'Treatment characteristics' section of the result (page 9):** "similar"→ "not different" **Line 4-5 of "Treatment-related AEs" section of the result (page 10):** "Other hematologic AE rates, including febrile neutropenia, were not different." **Line 6 of the first paragraph of the discussion (page 10):** "similar"→ "not different" **Line 1 of the last paragraph of the discussion (page 12):** "similar" → "comparable"
Reviewer #2 (00182891)	
it's an interesting paper about using modified dose of folfirinox. Results and statistical analysis were clear. this result give a strong conclusion	Thank you for your kind review and comments.
Reviewer #3 (01438231)	
This paper compares the effects of standard and modified doses of folfirinox used for the treatment of pancreatic cancer. The authors examined the efficacy and adverse effects. It is a well-presented, retrospective study performed in one institution. I suggest that the authors make sure to point out how this study differs from other studies that have compared to the standard and modified doses of these reagents, specifically references 13 through 17.	Thank you for your kind review and comments. 1) The strength of present study is that it is the first study that directly compared standard and modified dose of FOLFIRINOX. To point out this clearly, as you suggested, we made some changes. **Line 1 of aim in abstract (page 3)**: insert "directly" **Line 8-15 of the last paragraph of the introduction (page 5-6)**: "These research showed improved safety profile and comparable efficacy. Nevertheless, clinical feasibility or optimal strategy for dose-modification

The limitations of the study are presented on page 12. It would have been better to have equal numbers of patients in both groups, as well as a more even gender distribution, but this is difficult with respect retrospective studies. The data and statistical tests seem solid. The authors did find a significant reduction in adverse effects with the modified dose. Minor remark- The syntax is a bit awkward in the first and second paragraphs of the discussion and should be reviewed and reworded. Example-From manuscript: Therefore, our study could support the necessity of dose modification from the initiation of treatment, without compromising treatment efficacy, at least in elderly and female patients who have more concerns on treatment-related toxicities. Reworded: Therefore, our study supports dose modification from the initiation of treatment, without ...	of FOLFIRINOX still remains unclear, since previous studies on mFOLFIRINOX indirectly compared their results to those of PRODIGE4/ACCORD11 trial. Direct comparative study between standard-dose FOLFIRINOX (sFOLFIRINOX) and mFOLFIRINOX is still lacking. Therefore, in this study, we directly compared therapeutic efficacy and safety of sFOLFIRINOX and mFOLFIRINOX as first-line chemotherapy of PC." **Line 3 of the first paragraph of the discussion (page 10):** insert "direct" 2) We reworded and shortened some awkward sentences in the first and second paragraphs of the discussion. **Line 11-13 of the first paragraph of the discussion (page 10-11):** "Therefore, our study supports dose modification from the initiation of treatment without compromising treatment efficacy, at least in elderly and female patients who have more concerns regarding treatment-related toxicities." **Line 1-2 of the second paragraph of the discussion (page 11):** "Currently, FOLFIRINOX is a universally used first-line treatment for MPC, and it is also used for second-line or neoadjuvant treatment." **Line 4-5 of the second paragraph of the discussion (page 11): "**treatment-related AE is a major concern when using FOLFIRINOX."