Author's response to reviews

Title: Modified FOLFOX-6 chemotherapy in advanced gastric cancer: Results of phase II study and comprehensive analysis of polymorphisms as a predictive and prognostic marker

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Editor

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**Dear editor**

Manuscript number: MS 8888654301510560

We wish to express our gratitude to you and the reviewers for the pending acceptance of our manuscript entitled “Modified FOLFOX-6 chemotherapy in advanced gastric cancer: Results of phase II study and comprehensive analysis of polymorphisms as a predictive and prognostic marker”. We have tried to revise our manuscript based on the reviewers’ comments.

Here we have addressed the concerns of the reviewers on separate pages, as well as our responses to specific comments. I hope that you and reviewers will find these alterations satisfactory.

Best wishes,

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Thank you for your interest and acceptance of our manuscript. We revised the manuscript and yellow highlighted lines were marked in revised text. The followings are the comments of the reviewers and our responses to specific comments. Thank you very much for your consideration.

Reviewer: Annamaria Ruzzo
Minor Essential Revisions>
I think that C118T at page 6 must be changed in Asn118Asn. please verify throughout that all m-RNA have been changed in mRNA.
Response>
We revised our manuscript as reviewer’s recommendation.

Reviewer: Manuel Perucho
Small revisions>
1. ECOG performance (pg 5 and table 2) should be defined for the audience not familiar with the terms.
Response>
We described detailed explanation of ECOG performance status in page 5 line 12. We added one more references to explain ECOG performance status as reviewer’s recommendation. (reference number 27)

2. In page 7, ER should be changed for "enhancer region". The abbreviation is not necessary as it is mentioned only once. And it is difficult to remember the definition given at the beginning of
The conclusion that the chemotherapy protocol was "highly active" (pg. 8) and "highly effective" (pg. 11) should be toned down, as the response was relatively modest.

We have toned down the terms about efficacy. 'Highly active' was changed to 'active', and 'highly effective' was changed to 'effective'.

4. English still needs improvement. There are many incorrect or confused sentences. For instance, in the Discussion, the sentence "...while the results of other study conducted in Asian country [35] were concordant with our data", should be changed to "...while our results are concordant with those of another study conducted in an Asian country".

Similarly, "Contradictory, ..." (pg 10) should be replaced by "In contrast, ..." "These would be considered when interpretate predictive values of TS polymorphism" (pg 10) should be changed to "these experimental variables should be considered when interpreting predictive values of the TS polymorphism".

"Another considerable fact is the combined drug with 5-FU" (next sentence in pg. 10) should be changed to something like "Another fact to be taken into consideration is the possible impact on outcome of other drugs combined with 5-FU"...

Two sentences down, "This would make the meaningful polymorphism in single agent less significant in combination regimens" needs to be improved: "This would make the meaningful polymorphism in a single agent protocol less significant in combination regimens".

In next page (11), the sentence "In terms of 28-bp repeat polymorphism, loss of heterozygosity at the TS locus could occur in the genotype from a tumor tissue, in comparison with the genotype from a normal mucosal tissue [44]" is confusing. It should be better "In terms of the 28-bp repeat polymorphism, tumor-specific loss of heterozygosity at the TS locus has been reported [44]. "purely homogeneous" (pg 11) is redundant. Better "considerably homogeneous".

All of the reviewer’s recommendations were corrected. We received qualified professional English copy editing service to improve the style of English. Qualified professional English editing service named biomed proofreading (www.biomedproofreading.com). We thank Dr Stubbs, English editor of BioMed Proofreading for his assistance.