

Heraklion, 27/12/2013

Dear Editor,

Title: Prognostic and predictive significance of MSI in stages II/ III colon cancer

Authors: Zacharenia Saridaki, John Souglakos, Vassilis Georgoulas

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6321

Thank you for having reviewed our review article and providing us the experts' remarks. We would like to thank the reviewers for their constructive comments and suggestions.

Please find attached the revised version of our review (file name: 6321-review_Revised) which we would like to resubmit for publication in your journal. We have considered carefully all the reviewers' comments. All changes are highlighted yellow in the revised review article.

1. Format has been updated
2. References and typesetting were corrected
3. The following modifications were performed according to the reviewers' comments:

Reviewer 02445436

In this review, Saridaki et al. critically analyze the prognostic and predictive significance of microsatellite instability (MSI) in stage II colon cancer. Even if too brief, this review is updated and well written. Moreover, topics covered have clinical relevance. Major points: the division into paragraphs puzzles me. Biology is a paragraph of which, for example, "MMR system MSI definition – Hereditary and Sporadic Colon" and "Prognostic in stage II" are sub-sections? Titles of the paragraphs sound really strange (i.e. Prognostic in stage II, Hereditary and Sporadic Colon, Predictive...).

Answer:

Thank you very much for your comments. The rationale behind the selection of our paragraph titles had to do with the distinction behind the molecular/biology knowledge and the clinical prognostic and predictive one as far as the MSI phenotype is concerned. Based on your point we slightly altered our titles as seen in pages 5, 6 and 7.

Reviewer 02536716

This is the review paper dealing with the prognostic and predictive significance of MSI status in patients with stage II colon cancer. I think it is practical and important topic for the clinicians. This topic is not so novel, but valuable. Presentation and readability of the manuscript are good. I found no problems in ethics of the research. To make better review paper, I recommend a meta-analysis focusing on contrasting and combining results from different studies. And the author has to add a few recent papers (including *Annals of Oncology* 24:1274-1282, 2013). In the abstract, I found the wrong sentence "MSI should be evaluated be evaluated in stage II CRC patients". Please check.

Answer:

1. The scope of this manuscript was the presentation of the existing literature/ knowledge regarding the so interesting (according to our opinion) MSI phenomenon in CRC in the form of a critical review. Although, a meta-analysis of existing studies could be an interesting approach, nevertheless it is not among our intentions for the present manuscript.
2. Thank you very much for suggesting the reference "*Annals of Oncology* 24:1274-1282, 2013". Please, find it included among our reference list in pages 6 and in the References section page 13 (ref.25).
3. Thank you very much for this point. The redundant phrase "be evaluated" has been deleted from the abstract as seen in page 2.

Reviewer 02445660

Saridaki and colleagues reported the prognostic and predictive significance of MSI in colon cancer. A number of articles were used including MSI status between stage II and stage III CRC patients, and the potential effect of anti-cancer drugs in CRC patients. But there are a number of issues that need to be addressed: 1. The author list many cases including different standpoint whether it is necessary to use the MSI to be evaluated in stage II CRC patients. But the author did not draw a conclusion at the end of manuscript. Meta-analysis may be used to analysis these cases better than to simply listing these cases. 2. As a review paper, the author need refer to the more recent research. Some references are over 5 year-old. 3. In the conclusion, the author provided some methods to resolve the pending questions. Are there any recent progresses in the research of this field, for example "cheap biomarkers"? 4. A better title is needed to reflect the content in the text. The title is for "stage II CRC", but stage III CRC was also discussed in the manuscript.

Answer:

1. The scope of this manuscript was the presentation of the existing literature/ knowledge regarding the so interesting (according to our opinion) MSI

phenomenon in CRC in the form of a critical review. Although, a meta-analysis of existing studies could be an interesting approach, nevertheless it is not among our intentions for the present manuscript. Based though to your comment we have made our point and opinion much more clearly stated as seen in page 9.

2. Recent references have been added to our manuscript in pages 6, 7 and in the References section page 13 (ref 24) and page 13 (ref. 32), respectively.
3. In reply to your question, we have to state that according to our knowledge we are not aware of any recent progresses in the research of the field elaborated in the manuscript (for example in "cheap biomarkers").
4. Based on your very correct remark we improved the title by adding stage III, as seen in page 1 of the revised manuscript.

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

Sincerely yours,



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