

*To World Journal of Gastroenterology*

Dear Editors and Reviewers

I would like to thank you for the rapid and positive response to our manuscript entitled: "Nab Paclitaxel in pancreatic cancer: current evidences and future directions" (ID: 34134). After a careful evaluation of your comments, we have modified the manuscript as suggested. The new version of the manuscript contains one more author that is Dr. Tania Di Raimo, who has significantly contributed to the figure and tables assessment. The new version of the paper contains a figure, cited as figure 1 in the text, as requested by reviewer 1. This figure has been adapted from Celgene Corporation educational slides kit about nab - paclitaxel and we have obtained their permission to modify the figure. We attach the permission from Celgene to the revised version of the manuscript. Here we provide a detailed explanation of the modifications that you can find highlighted in the new version of the paper.

As suggested by the Editor:

- 1) We have attached to the manuscript the Language Certificate Letter by a professional English language editing company;
- 2) We have added Dr. Tania Di Raimo as a co-author because of her significant contribution to the revision of the article and to figure and tables assessment;
- 3) As a main author I confirm that my email address is the one that is reported in the paper because I use it as my principal mailbox address;
- 4) We have provided the audio core tip in mp3 file as requested;
- 5) We have added all the authors abbreviation names as requested;
- 6) We have modified all the references in superscript format as requested;
- 7) The reference list has been provided in the same form requested by authors guidelines and we have deleted all the repetitions in the references ;
- 8) We have added an acknowledgment sentence to Celgene Corporation for their kind permission to adapt figure 1 from their educational slides kit.

Here you are the responses to the Reviewers:

Reviewer n.1:

Comment: This review includes important of information about the use of nab-paclitaxel for the treatment of pancreatic cancer , such as background of PDAC, chemoresistance , results of clinical trials, and so on. the text is well written and helpful for clinical practice. Therefore, this article is suitable for publication. I would suggest only minor revisions, including the addition of 1) a figure of the proposed drug mechanism of action 2) some references to recent reviews on similar topics showing: - some potential avenues for further development in the metastatic setting and current efforts to integrate new effective chemotherapy regimens such as neoadjuvant, adjuvant, and multimodal approaches in both resectable and unresectable patients: Metastatic pancreatic cancer: Is there a light at the end of the tunnel? Vaccaro V, Sperduti I, Vari S, Bria E, Melisi D, Garufi C, Nuzzo C, Scarpa A, Tortora G, Cognetti F, Reni M, Milella M. *World J Gastroenterol.* 2015 Apr 28;21(16):4788-801 - the potential role of new biomarkers, including miRNA, to improve the selection of both nab-paclitaxel and Folfirinox

treatments in pancreatic cancer: FOLFIRINOX and translational studies: Towards personalized therapy in pancreatic cancer. Caparello C, Meijer LL, Garajova I, Falcone A, Le Large TY, Funel N, Kazemier G, Peters GJ, Vasile E, Giovannetti E. *World J Gastroenterol*. 2016 Aug 21;22(31):6987-7005.

Response:

We thank the reviewer for his positive comment and we have provided some modifications as requested. We have added a figure, cited in the text as figure 1, about the mechanism of action of nab - paclitaxel. The figure shows how nab - paclitaxel is carried through bloodstream after intravenous injection and then it is clearly showed the transcytosis mechanism related to the albumin-gp60/caveolin 1 pathway. Finally, the figure shows the interaction between nab - paclitaxel and SPARC proteins both on the pancreatic cancer cells and fibroblasts. We have also provided a figure legend in order to explain the different steps of this process.

As suggested by the Reviewer we have added the requested references in the text. Vaccaro V. et al article was cited into the text in the paragraph n.5 in the context of the discussion of the metastatic pancreatic cancer treatment landscape. This reference is reported as reference 68. In order to provide further insights about the role of potential biomarkers as predictive of resistance to pancreatic cancer treatments we have discussed and cited Caparello C et al article in the paragraph n.6. This reference is reported as reference 80 in the references list.

Reviewer n.2

Comment: This review deals with the role of nab-paclitaxel in pancreatic cancer treatment. This extensive review especially included an updated and critical information about the role of nab-paclitaxel in pancreatic cancer treatment. The nab-paclitaxel is a recently introduced drug which combined with gemcitabine regarding as a standard therapy in unresectable pancreatic cancer treatment. This paper will be helpful and useful for readers who want to know current status and new findings about the role of nab-paclitaxel in pancreatic cancer treatment.

Response: We would like to thank the reviewer for his positive comment

I hope that the revised version of the manuscript would meet the requirements for publication in *World Journal of Gastroenterology*.

Looking forward to hearing from you,

Sincerely yours

Dr. Guido Giordano

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