

Response to reviewers

Manuscript NO.:80214, Review

Title: Liquid biopsy leads to a paradigm shift in the treatment of pancreatic cancer

By: Fumiaki Watanabe

Dear Professor

Thank you very much for your letter dated October 9th, 2022, with the detailed and constructive comments from reviewers on our submitted manuscript entitled “Liquid biopsy leads to a paradigm shift in the treatment of pancreatic cancer”.

We agree that the manuscript is much improved after incorporation of reviewer’s comments, and we have amended the manuscript accordingly. The answers to all the comments by reviewers are described in the following pages of this letter, saved as a 'Answering Reviewers' file. Reviewer’s original comments are shown in blue. My responses are shown in black and each modified point is shown in red with an underline in the text..

Sincerely yours,

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General comments:

Reviewer #1

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: An interesting, well-written review of liquid biopsy in PDAC patients, I think perhaps a greater comparison with CA 19.9 might be useful. I believe that these two works should be cited in this sense: - Coppola A., La Vaccara V., Fiore M., Farolfi T., Ramella S., Angeletti S., Coppola R., Caputo D. CA 19.9 Serum Level Predicts Lymph-Nodes Status in Resectable Pancreatic Ductal Adenocarcinoma: A Retrospective Single-Center Analysis. *Front. Oncol.* 2021; 11: 690580. doi: 10.3389/fonc.2021.690580. - Luo G., Fan Z., Cheng H., Jin K., Guo M., Lu Y., Yang C., Fan K., Huang Q., Long J., et al. New observations on the utility of CA19-9 as a biomarker in Lewis negative patients with pancreatic cancer. *Pancreatology.* 2018; 18: 971–976. doi: 10.1016/j.pan.2018.08.003

We agree with the reviewer's suggestion.

In response to the reviewer's suggestion, we cited two references in the manuscript as follows:

Carbohydrate antigen 19-9 (CA19-9) is considered the best tumor marker for patients with PDAC. CA19-9 values correlate with tumor size, stage, and burden^[17, 18].

Although CA19-9 is a helpful prognostic factor of PDAC, its usefulness remains controversial^[19, 25-27]

18 Coppola A, La Vaccara V, Fiore M, Farolfi T, Ramella S, Angeletti S, Coppola R, Caputo D. CA19.9 Serum Level Predicts Lymph-Nodes Status in Resectable Pancreatic Ductal Adenocarcinoma: A Retrospective Single-Center Analysis. *Front Oncol* 2021; **11**: 690580 [PMID: 34123859 PMCID: PMC8190389 DOI: 10.3389/fonc.2021.690580]

27 [Luo G, Fan Z, Cheng H, Jin K, Guo M, Lu Y, Yang C, Fan K, Huang Q, Long J, Liu L, Xu J, Lu R, Ni Q, Warshaw AL, Liu C, Yu X. New observations on the utility of CA19-9 as a biomarker in Lewis negative patients with pancreatic cancer. *Pancreatology* 2018; **18**\(8\): 971-976 \[PMID: 30131287 DOI: 10.1016/j.pan.2018.08.003\]](#)

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors well summarized the status, clinical efficacy, limitations, and further perspectives of liquid biopsy on pancreatic ductal adenocarcinoma. Language quality is also good.

Thank you for your review and comments. We have carefully reviewed the English language of our manuscript including punctuation, conjunction and article related errors, and have addressed these in our revised submission.