

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 05449007

Position: Peer Reviewer

Academic degree: MBBS, MD

Professional title: Academic Fellow, Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-28 22:58

Reviewer performed review: 2021-01-28 23:24

Review time: 1 Hour

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I would like to congratulate the authors for an extremely well-written and thorough review on second-line treatment of pancreatic adenocarcinoma. The authors do a phenomenal job of reviewing the current literature on this topic and also highlight future directions in the field. I have only minor edits to suggest for this excellent review: 1. Grammar can be improved. Reduce redundancy as there seem to be some repetition in initial paragraph 2. Use only standard abbreviation and please mention full form along with the abbreviation in first use. 3. Consider adding the following citation in the section of targeted therapy or future directions as this review from JAMA oncology highlights future prospects of germline mutations in PDAC. This citation should be a great addition to your well written review. "Rainone M, Singh I, Salo-Mullen EE, Stadler ZK, O'Reilly EM. An Emerging Paradigm for Germline Testing in Pancreatic Ductal Adenocarcinoma and Immediate Implications for Clinical Practice: A Review. JAMA Oncol. 2020;6(5):764-771. doi:10.1001/jamaoncol.2019.5963"

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 03872428

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-26 22:38

Reviewer performed review: 2021-01-30 12:16

Review time: 3 Days and 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The present review describes the controversial and unsolved topic of second-line treatment of advanced pancreatic cancer. I think that this review is well-written and suitable for publication in World Journal of Gastroenterology. I believe the paper will be of interest to the readership of World Journal of Gastroenterology and would recommend it for acceptance after the minor point listed below are addressed. Minor

1.Introduction section: Please spell out the PDAC.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 02803865

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: France

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-01-27 08:00

Reviewer performed review: 2021-02-01 13:52

Review time: 5 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors report a review on second-line treatment of pancreatic adenocarcinoma. The topic is of interest. The manuscript requires revision for publishing. Complex sentences (more than 1 idea) should be simplified: 1 idea/1 sentence. Ex "To date, chemotherapy is still //, unfortunately providing //", "Precision médecine could be the key // and finally imacting Survival //". Standard requirements should be fulfilled: page numbering (and/or continuous line numbering).

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 05463920

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-29 01:53

Reviewer performed review: 2021-02-08 09:14

Review time: 10 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The topic selection is a good thing, the manuscript information is large, and the author arranges the literature in an orderly way, but most of the content is extracted from the results of others (including test results and Statistics), and the article lacks the author's simplest comments on these results. The following suggestions are put forward: 1) The author only "states" but not "comments", which should be the organic combination of "states" and "comments", that is, "states" is the basis of "comments", and "comments" is the extension and improvement of "states". Therefore, at the end of each segment, after the author introduces others' academic views and research results, the author also needs to briefly summarize the information, clarify your personal opinions, and put forward the necessity and theoretical value of further research in this field. 2) Abbreviated terms have to be explained in full name when they first appear. The author should know that this is the foundation for writing. Clean up all abbreviations, including but not limited to the following: OS, PS, ORR, NAL-IRI, nab-paclitaxel, NTRK, BSC, OFF, FF, XELOX, FOLFOX, CapeOX, ECOG, etc. 3) Supplement the standard of first-, second- and/or third-line therapy. Let the reader know clearly when to use what kind of treatment. 4) The term "pancreatic cancer" is quite confusing in the manuscript. Such as: pancreatic adenocarcinoma (title), metastatic pancreatic ductal adenocarcinoma (PDAC) (paragraph 1 of Section 2.1), metastatic PDAC (section "1. Introduction"), PAC (no full name, 3.2 section), advanced pancreatic cancer (Section 2.2), metastatic PAC (paragraph 1 of section 3), MPDAC (Paragraph 3 of section 2.1), mPDAC (Section 4), etc. The author's expression of the terms should not change with the change of the literature, and the same manuscript should have consistent terminology expression. Please unify the term. In addition, there should be a brief introduction to the classification of PAC. 5) Table 1 is not so much a table as a figure. So, change it to a figure and add a figure legend. In addition, what mean does the last "clinical trials" on the left? Figure 2 also

needs to add a figure legend. 6) The subheadings should be consistent, for example, in the "1) Second-line chemotherapy after treatment with FOLFIRINOX " section, a) is "gemcitabine in monotherapy", b) should be "gemcitabine based combination therapy", not "gemcitabine based treatment"; in the "2.2 TARGETED THERAPY " section, "Erlotinib" should correspond to "Larotrectinib and entrectinib" instead of " TRK inhibitors in TRK fusion-positive cancers: Larotrectinib and entrectinib", or change "Erlotinib" to "EGFR TI inhibitor: Erlotinib". Please check the full text and revise it. 7) For "future directions", the author mentioned "increase of targeted therapies". What is the basis? Do you have the most promising therapeutic targets and drugs? Yes, what is it? Please be clear. 8) Note that some expressions are not well, such as "44-48%" and "62-65%", the correct writing should be "44% - 48%" and "62% - 65%"; Table 2 has no table header.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 03872428

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-03-10 03:28

Reviewer performed review: 2021-03-10 05:03

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The present review was well revised and is acceptable.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 62770

Title: Pancreatic adenocarcinoma: Beyond first line, where are we?

Reviewer's code: 05463920

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-26

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-03-10 01:36

Reviewer performed review: 2021-03-10 07:57

Review time: 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1. To clarify the concept, the author used the term "pancreatic adenocarcinoma" in the



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title, the term "pancreatic cancer" in the beginning of the abstract, and the term "pancreatic ductal adenocarcinoma (PDAC)" in the Core tip section. The meanings of the three terms are not really the same, which is why I hope the author will give a classification of pancreatic cancer. The author should distinguish the relationship between the three terms. The term "pancreatic adenocarcinoma" is also called "pancreatic cancer" by many scholars, so they are the same ones concept. Pancreatic ductal adenocarcinoma (PDAC) is the most common pancreatic adenocarcinoma(pancreatic cancer), accounting for about 80% - 90%. 2. In subtitle "2. CURRENT CLINICAL PRACTICE IN SECOND LINE METASTATIC PAC" and "3.2 Increase of targeted therapies" section. The abbreviated term "PAC" should be changed to PDAC. Similarly, the "MPAC" in "3. FUTURE DIRECTIONS" section should be changed to mPDAC. 3. In the third natural paragraph of "2.1 CHEMOTHERAPY" section, what is the abbreviation MPACT? There should be an explanation. 4. "In conclusion, on the first-line treatment used . Within the 5FU-based regimens," , there is an extra space after the word "used". Similarly, in the second paragraph of "larotrectinib and entrectinib" section, the word "sustainability" is followed by the same thing, while the word "contexts" is followed by a blank space.