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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65674

Title: Importance of BRCA mutation in the current treatment of pancreatic cancer beyond maintenance

Reviewer's code: 05242567
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: Spain

Manuscript submission date: 2021-03-16
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-03-17 02:40
Reviewer performed review: 2021-03-24 17:49
Review time: 7 Days and 15 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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SPECIFIC COMMENTS TO AUTHORS

The editorial by Martínez-Galán is well written and is a timely topic related to therapeutic guidance involving molecular profiling involvement of PC patient management. Several comments are provided. 1. Page 4, first paragraph, "…had more favorable prognoses…real-life clinical setting…": Would specify however that comparative populations were still matched. 2. Page 4, second paragraph, "…whose mutation has…outcomes in PC…": Would expand and provide specific benefit and trial design (i.e., retrospective and very small number of patients). 3. Page 6, first paragraph, "…obtain a major…": still limited proof to be major benefit. Although seems worth further study in BRCA mutant and/or deficient profile. 4. Page 6, second paragraph, "In a retrospective study of 36…p = 0.04).": Add to upfront. 5. Page 7, end of third paragraph: It is also published by others involving ovarian cancer that alternative therapy involving BRCA-wt profile may also be considered as optimal (RP Rocconi et al Gynecologic Oncology 2021) thereby further justifying separation of therapy based on BRCA deficiency or not.

POINT-BY-POINT RESPONSES TO REVIEWER

1. Page 4, fourth paragraph: We now provide more specific information on this issue as follows:

   "However, it should be taken into account that participants in the PRODIGE4/ACCORD11 study had a more favorable prognosis and were less representative of the real-life clinical setting in comparison to those in the MPACT study. Specifically, 37% of the former had a functional ECOG score of 0 versus 16% of the latter, the tumor site was the pancreatic head in less than 40% of patients versus 60-65% in clinical practice and 44% in the MPACT study, there was an average of two metastatic

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sites in patients in the PRODIGE4/ACCORD11 study versus three in the MPACT study, the CA 19-9 marker was elevated in 42% of the former versus 52% of the latter, and no patient over the age of 76 years was included in the PRODIGE4/ACCORD11 study. We also highlight that the higher survival and response rates in FOLFIRINOX-treated patients were accompanied by a significant increase in hematologic and non-hematologic toxicity, explaining why FOLFIRINOX is often administered at a reduced dose or in modified form in the clinical setting."

2. Page 5, second paragraph: As requested, we have expanded our description of this trial as follows:

   "This evidence derives from multiple in vitro studies and was supported by a clinical trial that found a longer overall survival (14 vs. 5 months; hazard ratio [HR] = 0.58; P *= 0.08) in advanced PC patients treated with platinum-based regimens who were carriers of BRCA mutations than in those who were not, although this was a retrospective study in a sample of only 12 patients (n = 12)*[17]*."*

3. Page 7, second paragraph: This sentence has been changed accordingly, and also note that further research is warranted on *BRCA* mutant/deficient profiles as follows:

   "According to these findings, a substantial sub-population of patients with PC can benefit from platinum-based regimens, although the underlying molecular mechanisms have not yet been elucidated and further research is warranted on BRCA mutant/deficient profiles".

4. Page 7, third paragraph: This information is now presented earlier in the paragraph.

5. Page 9, second paragraph: As suggested, we now cite the study by Rocconi et al.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65674

Title: Importance of BRCA mutation in the current treatment of pancreatic cancer beyond maintenance

Reviewer's code: 03104669

Position: Peer Reviewer

Academic degree: FACS, MD, PhD

Professional title: Director, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Spain

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Reviewer chosen by: Ya-Juan Ma

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

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SPECIFIC COMMENTS TO AUTHORS

In the editorial entitled" Importance of BRCA mutation in the current treatment of pancreatic cancer beyond maintenance" the authors demonstrate the BRCA gene status of patients with pancreatic cancer among clinical criteria for the selection of first-line chemotherapy regimen. The editorial has an excellent summary and claims publishing.

POINT-BY-POINT RESPONSES TO REVIEWER

We are grateful to the reviewer for this positive assessment.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65674

Title: Importance of BRCA mutation in the current treatment of pancreatic cancer beyond maintenance

Reviewer's code: 03738819

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Spain

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

The authors discussed the importance of BRCA mutations in pancreatic cancer and concluded that BRCA mutations could be used to select the optimal first-line treatment regimens. Generally speaking, this manuscript could be published in the "World Journal of Gastroenterology" after some minor revisions. 1. The abbreviation of PARP inhibitor would better change to PARPi. 2. In line 9 on page 7, we suggest that the authors briefly introduce the content of literature 22, therefore the process of drawing conclusions will be more logic.

POINT-BY-POINT RESPONSES TO REVIEWER

1. The abbreviation of PARP inhibitor has been changed to PARPi.
2. Page 8, second paragraph: As requested, we have added the following information:

"In this regard, a meta-analysis[22] of studies comparing the response to PARPi included eight studies that showed a response to PARPi in 24 out of 43 patients (55.8%) with somatic BCRA mutations and in 69 out of 157 patients (43.9%) with germline BCRA mutations (43.9%), a non-significant difference (P = 0.399). It also included five studies that reported no difference in PFS between patients with somatic versus germline BCRA. The authors concluded that the response to PARPi therapy is similar between these types of patient."