

## Peer Review File

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### Reviewer A

In the present manuscript, Rubinson and colleagues describe the interesting case of a metastatic pancreatic cancer female patient first randomized to the placebo-arm of the POLO trial (phase 3 trial testing efficacy of PARP inhibitor olaparib maintenance therapy on platinum-sensitive germline BRCA-mutated PDAC) who faced cancer progression on placebo. After being taken off the POLO trial, the patient's tumor responded again well to FOLFIRINOX. The patient was then started on off-protocol maintenance olaparib. The last 48 months, her cancer displayed durable complete response, as shown by her normal CA 19-9 levels, throughout the course of olaparib therapy. The patient also reported a good tolerance to the treatment with an excellent quality of life. This case report further highlights that PARP inhibitor maintenance therapy is highly potent in appropriately selected metastatic PDAC patients.

Overall, the case is well-described, provides novel clinical insights on the topic, and includes appropriate and interesting discussion on an active topic of clinical cancer research. Some minor points must be addressed before publication, to improve the quality of the article.

#### Minor points

1. The sentence page 2 line 8 to 12 (abstract section) is 100% similar to the sentence page 4 line 23 to 26 (introduction section). The authors should rephrase one or the other in the final version of the manuscript.

**Thank you very much. We made this correction. We added changed the redundant sentence in the introduction to the following:**

*In this report, we describe a patient with germline BRCA2-mutated, metastatic PDAC who has benefited from maintenance olaparib for over 4 years. Importantly, the patient's previous progression on the placebo arm of the POLO study serves as an internal control clearly demonstrating the benefit of maintenance PARP inhibition in this case.*

2. The sentence page 4 line 15 to 18 could be split in two sentences and rephrased for better clarity.

**Thank you very much. We made this correction. We added changed the redundant sentence in the introduction to the following:**

*Her cancer responded well to FOLFIRINOX. Radiologically, there was an 89% reduction in her tumor volume, per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, with a 67% reduction in the size of her pancreatic mass and a complete response in the abdominal wall nodule (Figure 2).*

3. Figure 1 and 2 are presented in low resolution. Can the authors provide them in a higher resolution? Moreover, the size of Figure 2 is inadequate for a correct visualization of the details. This must be adapted. The arrows are indeed (and also) not visible at all.

***Thank you very much. We revised Figure 2 with higher resolution radiology images. In addition, we enlarged the size of each of the radiology images and added red arrows. Figure 1 is at its maximum resolution.***

4. Page 4 line 4-5, the authors gave a second time the meaning of “FDA”. This can be removed.

**Thank you very much. We made this correction.**

***PARP inhibitors have since been approved by the FDA for the treatment of HR-mutated breast and prostate cancers (15, 16).***

5. The meaning of “CT” and “FOLFIRINOX” is missing in the legend of Fig. 2.

**Thank you very much. We made this correction.**

***Computed tomography (CT) scans demonstrating the radiological response of the pancreatic tumor to therapy over the course of treatment. Arrows indicate the location of the pancreatic tumor. Abbreviations: 5-fluorouracil (5-FU), leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX).***

6. The article title should mention the term “case report”, according to CARE guidelines.

**Thank you very much. We advocate for leaving the title as it is. The title clearly defines the manuscript and makes it clear that we are discussing an individual case. This manuscript is both a description of the clinical case and the molecular genetics of the patient. The molecular aspects of this case are why it is important. Given the molecular nature of the report, we think adding the phrase “case report” might prevent basic scientists from reading this.**

7. The section title “conclusion” should be replaced by the term “discussion”.

**Thank you very much. We made this correction.**

8. The page numbers/line numbers reported in the CASE checklist do not match with the page/line numbers in the manuscript.

**Thank you very much. We updated to this and included it with this resubmission.**

**Reviewer B**

Nicely written. It is an ongoing hot topic. If it was something about resistive pathology, it would have been more interesting

### Reviewer C

This is a well-written and interesting case report that describes a patient with a germline BRCA2-mutated, metastatic pancreatic cancer. After progressing on the placebo-arm of the POLO study, her cancer responded to platinum- based chemotherapy and has since been successfully treated for 4 years with off-protocol maintenance Olaparib. The results will be of high interest to scientists and clinicians in the field of pancreatic cancer research, PARP inhibitors, and other HR mutated malignancies such as ovarian cancer. There is little to criticize here. Only a few minor suggestions:

Figure 2- can the authors enlarge the image panels, make the arrows a different color so it is easier for readers to visualize the pancreatic tumor mass?

*Thank you very much. As mentioned above, we revised Figure 2 with higher resolution radiology images. In addition, we enlarged the size of each of the radiology images and added red arrows. Figure 1 is at its maximum resolution.*

Figure 2 - Can the authors graph the tumor volume in addition to showing the images?

*Thank you very much for this comment. We attempted doing this but felt that the volumes measurable might be deceptive and misleading the reader.*

Discussion - Perhaps comment on the likelihood that there is tumor eradication in this patient, if the patient is alive currently and if so, will she remain on Olaparib indefinitely?

**Thank you very much for this comment. In our estimation, we do not think the tumor is eradicated and our plan is to continue the olaparib indefinitely. We added the text below to the manuscript.**

*Given her excellent tolerance on olaparib, the therapeutic plan is for her to continue on olaparib indefinitely as long as it continues to control her cancer.*