

Answering Reviewer 1:

For point 1:

- 1) The chemotherapy modified FOLFIRINOX(mFFX) was given in 2-weekly schedule based on BSA  $1.77\text{m}^2$ . I had described the chemotherapy dosing and calculations in full detail in section "Treatment".
  - 2) The elevated transaminases level was mild. The AST, ALT and Total Bilirubin values were added in the section "Laboratory Examination".
  - 3) First CT evaluation was performed after completion of 2 cycles. After that, CT imaging was performed at timepoint post 4<sup>th</sup>, 8<sup>th</sup> and 11<sup>th</sup> cycles. I had added the description of imaging results in the section "Outcome and Follow up".
  - 4) The only side effect that the patient experienced was Grade 1 peripheral neuropathy, which increased with subsequent cycles of chemotherapy leading to the decision of chemotherapy discontinuation ultimately. Besides from that, he has no other significant toxicities. In fact, he was generally improved symptomatically with the chemotherapy effect. This is described in the sections "Outcome and Follow up" and "Discussion".
  - 5) The detail of the PARP inhibitor had been added to the section "Outcome and Follow up".
  - 6) The Ca19.9 level was normal at presentation. I had revised this information to make it clearer in the section "Laboratory examinations".
- I also make it clearer that the diagnostic histology examination did not reveal a mixed subtype in the section "Final diagnosis".

2) This is main message of our case report, as outlined in the "Abstract" and "Discussion" sections. We want to stress the importance of genomic profiling which had helped the management of this challenging case. Although our case was very unwell with poor health condition at presentation, raising the question of suitability for modified FOLFIRINOX, the knowledge of the *BRCA2* LPV as predictive for platinum sensitivity had confidently guided our decision to use this regime which ultimately resulted in patient's improved outcome. I had made this point clearer in the sections "Abstract" and "Discussion".

The patient's tumour regression was deepening with chemotherapy as seen with the interval scans, we did not stop our patient's chemotherapy at earlier timepoint (i.e., cycle 4 or 6). Furthermore, he had good tolerability to modified FOLFIRINOX. Based on the POLO trial's data, patients are often de-escalated to maintenance therapy with PARP inhibitors after 16 weeks of induction chemotherapy. I made all these points clearer in the 7<sup>th</sup> paragraph in section "Discussion".

3) I had briefly described and added the association between germline *BRCA1/2* mutations and familial pancreatic cancers in the 3<sup>rd</sup> paragraph in section "Discussion".

4) The submitted IRB statement is for a COMPASS (Comprehensive Molecular Characterization of Advanced Pancreatic Ductal Adenocarcinoma for Better Treatment Selection) This is a prospective study designed to increase accessibility to

comprehensive WGS and RNA sequencing for all patients with clinical diagnosis (radiological) of pancreatic cancers at enrolment. Majority patients are ductal adenocarcinomas, however in rare circumstances we discovered different subtypes such as acinar cell carcinomas that are also profiled.

For this paper, we had completed extensive literature search and included latest references/citations to support the paper content.

Finally, I want to indicate again that the manuscript is a case report and case series with a shared discussion. The automated manuscript editor is for case report only (I was unable to arrange the case series, which is after the case report).

Yours sincerely,

Dr Cha Len Lee