Reviewer's report

Title: A retrospective study of neoadjuvant FOLFIRINOX in unresectable or borderline-resectable locally advanced pancreatic adenocarcinoma

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Reviewer: Paula Ghaneh

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Comments:

1. In the introduction the authors state ‘Radiation therapy has also been shown to be beneficial in patients with LAPC and combined chemoradiotherapy (CCRT)’. There is no level one evidence for this – could the authors qualify this statement and say that prospective randomised trials are ongoing to evaluate whether there is a survival benefit of CRT versus systemic chemotherapy.

2. In the ACCORD trial there were a high proportion of patients with body tumours, not jaundiced and with good performance status. An important outcome for this study would be to look at the complications and toxicity for patients with head tumours and jaundice. The authors could highlight that in the introduction/discussion.

3. The authors need to describe their aims and outcome measures more clearly at the end of the introduction (these are listed in the methods but a small sentence here would be useful).

4. As there is no internationally agreed definition of locally advanced/unresectable and borderline resectable pancreatic cancer – it is really important that this group is very clear on their definitions and although they are treating them in the same way – for the outcomes such as resection rate etc the two groups need to be described separately.

5. Tumors were defined as UR if there was extensive peripancreatic lymph node involvement – we would not define this as unresectable. Could the authors perhaps include a table of the exact criteria of unresectability and borderline unresectability?

6. In the methods section, I am not clear what criteria was used for response - RECIST1.1? Could the authors clarify maximum response and tolerability?

7. Did the authors have a prescribed number of cycles for their therapy – it is not clear?

8. How soon after completion of therapy did the patients undergo resection?

9. The primary endpoint was R0 resection rate – how is this defined? Tumour at or less than 1mm from the resection margin R1?

10. Statistical analysis includes Kaplan Meier survival curves – was there an event rate to be reached before analysis? The numbers are very small so
univariate analyses of any prognostic factors will be fraught with problems and may not be difficult to interpret. Also the authors should state that descriptive statistics were used for data.

11. In the results section - in Table1 – basis for unresectability should be divided into what the authors thought was unresectable and borderline resectable.

12. Were the stents covered metal or plastic – any complications associated with the stents – eg. cholangitis – could the authors comment?

13. The flow chart groups the patients together (UR and BR) it would be informative to have the flow for UR and BR patients separate so we can see the outcomes.

14. The survival curves should be altered – to one overall survival curve and another demonstrating the survival of those patients who had a resection and those who did not. The numbers at risk should be along the x axis.

15. The main interest at this stage for specialists is the feasibility and toxicity of this regimen in this group of patients. Therefore it cannot be stressed too much that the discussion needs to highlight the toxicity and complications of this approach as this information is very important and vital for future studies.

16. The authors also need to highlight the very short follow up which makes interpretation of the data difficult. Such as analysing R1 and R0 survival differences.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests'