Peer Review File

Article Information: https://dx.doi.org/10.21037/jgo-23-488

Reviewer A

Comment 1: The authors collected rather large series of institutional data of the patients with pancreatic cancer. However, the results presented just showed the survival according to the disease extension (localized vs. metastatic) with no novel findings. Although the primary and secondary regimens were presented, the dose intensity or at least duration of the treatment should be presented as background data. Each of the two groups presented in Figure 1 included highly heterogeneous patients in terms of tumor resectability, T or N category, or response to chemotherapy. I would recommend for example presenting the background and survival outcomes of the patients who received only chemotherapy, chemo plus radiation, and surgery.

Reply A: Many thanks for your comments. We have now included dose intensity (page 6, lines 194 to 196). We have also included a table of background and survival outcomes based on those who received chemotherapy, chemo plus radiation and surgery as suggested. (page 5, line 167 to 168)

Reviewer B

This is a retrospective, single Center analysis of treatment of pancreatic cancer in Western Australia. the paper is interesting and shows impressing survival results in patrients with locally advanced (?) and metastatic pancreatic cancer treated with multimodality therapy. However, I have some issues which need to be clarified.

1- I presume that the paper is devoted to locally advanced or metastatic pancreatic cancer. However, the Authors report in the text locoregional, locally advanced, resectable, border-line resectable and metastatic pancreatic cancer. There is some confusion about the terms and which patients are effectively included in the study.

2-Survival of patients with locally advanced and metastatic pancreatic cancer appears too long in this study and may suggest a selection bias.

3- Some patients underwent chemotherapy and surgery in different combination: the rate of down staging and the type of surgery are not reported. I think these informations are interesting for the readers.

Reply B:

1- This paper mainly focuses on locally advanced or metastatic but also includes 34 patients who were borderline resectable and subsequently had surgery. We have now clarified the terms and ensured they are consistent throughout the paper.
2- We agree that selection bias is a limitation and we have mentioned this in the discussion of the study (page 10, line 370)
3- We have now included more details on surgical patients (page 5, line 184-186)

Reviewer C

Manuscript Summary:
In this manuscript, the authors present a retrospective cohort study evaluating the survival outcomes of patients with pancreatic ductal adenocarcinoma (PDAC) over a 13-year period in a single center in Western Australia. PDAC is known for its aggressive nature and low survival rates, but recent advancements in standard-of-care chemotherapy have shown promise in improving outcomes.

The study highlights the favorable survival outcomes observed in Western Australia, possibly attributed to access to modern therapies and diagnostic technology. However, the authors acknowledge certain limitations of the study, such as its retrospective nature and lack of a direct comparative arm with global data. Please find details comment below.

Major Concerns:
1.
111 Treatment modalities varied broadly between patients depending on age, disease extent, performance
112 status at diagnosis, patient preferences regarding intensity of therapy and suitability for clinical trials.

The study would benefit from a clear and structured description of treatment algorithms and protocols used for the treatment of patients with different disease stages and surgical resectability status.

2. "Western Australia has shown favorable survival outcomes compared to global standards."
- I do not think this is an appropriate conclusion to draw based on retrospective single-center experience and no definition of global standards.

3. More data on the survival of different patient cohorts with different treatment modalities and even chemotherapy regimens is needed. Please also provide data on surgically treated vs non-surgical treatment.

4. 68 or metastatic disease. Pancreatic neuroendocrine tumours were excluded.
There is no need to specify that neuroendocrine tumors were excluded, given that you only studied PDAC. Diagnostic criteria for PDAC as well as other exclusion criteria used, would be helpful to understand the methodology of the study.

Minor Concerns:
1. A description of “adequate” performance status should be provided using ECOG or other classification/scoring system
2. Please provide a description of what the authors mean by locoregional disease.

3.
63 …extracted from an online medical oncology database.

-This should be specified in the methods section, which database is used?

4.
131 …and only one patient successfully down-staged to allow subsequent surgical intervention.
- Could you provide more details on this case, such as the location of the primary tumor, the location of metastatic disease (and was metastasis pathologically confirmed?) and treatment given (chemo type, number of cycles)? This would be of great interest due to the rarity of down-staging of metastatic disease and surgical treatment of this group of patients

5. Regimens for neoadjuvant chemotherapy (chemo type, length, etc), as well as indications for latter(locally advanced disease, borderline resectable disease?), should be specified.

Reply: Thank you for your comment. We have now included neoadjuvant therapy details. (See line 147-149, page 5)

Changes in text: There were 34 patients who received neoadjuvant chemotherapy (31 Gem/NabP, 3 FOLFIRINOX,) Median length of neodjuvant therapy was 4 months (range 2-11 months).

Reply C:
Major concerns:

1- We have now included protocols / treatment algorithm (see page, line) and have made the terms consistent throughout the paper. (page 6, lines 194 to 196).
2- We have amended the conclusion to avoid overestimating results from a retrospective study (page 10, line 376).
3- We have now included more data on chemotherapy and surgical regimens (page 5, line 167 and page 5, line 184-186)
4- We have amended the methods as suggested (page 2, line 67-70).

Minor concerns:

1- We have included specific ECOG scoring (page 9, line 378).
2- We have amended terminology and ensured consistency throughout.
3- We have amended the methods to include specific description of oncology database used (page 2, lines 69-70)
4- Patient X was diagnosed with a tail of pancreas lesion, peripancreatic and paraaortic nodal disease with nodal infiltrate adjacent to coeliac trunk and porta-hepatis. They were treated as locally advanced disease. This patient was erroneously documented as metastatic at diagnosis in our database as following her chemotherapy , radiation and salvage surgery she developed liver metastasis confirmed at biopsy that initially were thought to be benign cysts. In retrospect she may have had early metastatic disease at diagnosis however she was been initially treated as locally advanced and we have therefore amended our results accordingly including her in our non-metastatic at diagnosis group.