

## Responses to the reviewers' comments

### Reviewer 1

The authors examined the clinical history of  $\geq 5$ -year survivors with non-resected pancreatic adenocarcinoma. The manuscript is well written and the topic is interesting for the readers of World Journal of Gastroenterology. I suggest some changes to make the manuscript suitable for publication.

1. Please re-write the core tip because is too similar to part of abstract.

Please see the revised core tip in the manuscript.

2. For the pancreatic cancer progression is very important the role of immune response as suggested by different studies (PMID: 23640603, PMID: 25483688). Please cite the manuscripts and discuss this point in discussion section.

Please see the revised manuscript. We have cited the references and discussed the potential role of immune system in the progression of pancreatic cancer and novel immunotherapy in the treatment of pancreatic cancer.

3. In the table is absent the immunological parameters of patients, such as cancer infiltration of immune cells (in particular T cells) and the distribution of the different leukocyte subsets in the peripheral blood. Please provide to add them in the tables.

Please see the neutrophil-to-lymphocyte ratio in the peripheral blood in Table 2. Regrettably, we cannot assess the leukocyte subsets within the tumors, as 9/11 cases have no tissue block or no tissue remaining in the blocks, and 2/11 have tissue blocks which were too small for further analysis. However, we agree that immunological parameters of pancreatic cancer patients warrant further research and may play a significant role in determining the response to therapy and long-term survival.

## Reviewer 2

This manuscript report clinical features of long-term survivors of pancreatic adenocarcinoma without curative resection. This case series are well written. The features of long-survivors are detailed. However, I several concerns are raised below.

1. Authors merely described detailed features of long-term survivors. I recommend authors to analyze which factors are related to long-term survival.

Given the limitation of a case series and that we do not have detailed information of non-resected patients who survived less than 5 years for comparison, it is difficult to define the characteristics associated with the long-term survivors. Nevertheless, based on our observation, the majority of the long-term survivors were younger than 70 years of age, exhibited excellent performance status and had tumors in the head of the pancreas, which were previously identified as favorable prognostic factors in pancreatic cancer<sup>[30,31,32]</sup>. Additionally, patients were prone to significant morbidities, such as recurrent cholangitis, liver abscess, malnutrition, second malignancy and small bowel perforation (Table 2). Lastly, patients with disease progression responded favorably to second-line chemotherapy, even though most of them received the regimen identical to the initial therapy. Ultimately, it would be worthwhile to define the predictors of long-term survival via a multivariate analysis by comparing these long-term survivors with those who survived less than 5 years without resection.

2. The pathological diagnosis is very important in this study, because misdiagnosis of pancreatic adenocarcinoma seemingly lead to the long-term-survival. Therefore, authors should mention detail of pathological diagnosis of all 11 patients. Was EUS-FNA was used for sampling? Was pathological diagnosis obtained from pancreatic mass or metastases? Cytology or histology? Did authors exclude endocrine tumors and autoimmune pancreatitis?

EUS-FNA for cytology of a pancreatic mass was performed in 7, ERCP brushing of the bile duct for cytology in 1, pancreatic core needle biopsies in 2 and a core needle biopsy of a pyloric mass/implant in 1 patient. Autoimmune pancreatitis, neuroendocrine tumors and tumors arising from the bile duct, gallbladder and duodenum were excluded by a gastrointestinal pathologist after a second review of all the specimen.