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Re: Contribution of pancreatic enzyme replacement therapy to survival and quality of life in patients with pancreatic exocrine insufficiency

To the Editorial Office,

On behalf of myself and my co-authors, we are pleased to enclose the above referenced manuscript for resubmission to *World Journal of Gastroenterology*.

We thank the reviewers for their insightful comments and we believe that these have now been fully addressed, where possible, in this revised version of the manuscript. Please find detailed responses to each comment in the table at the end of this letter.

In addition to addressing these comments, we have implemented all the style changes requested by the Editor. Of note, we have moved the information on methodology and all the tables to the Supplementary Information.

All alterations we have made have been clearly denoted by tracked changes and highlighted text in the enclosed revised manuscript.

We hope that the manuscript now meets the requirements of *World Journal of Gastroenterology* and look forward to hearing from you at your earliest convenience.

Respectfully,

Professor P. Layer, MD

Reviewer comments

- This is a well-designed, clinically important review which contains 70 references. It seems that figures were re-designed using the data from cited references. There are 4 figures and 8 tables which are clear and informative. Authors highlight underuse (21-43%) and under-dose in daily practice of pancreatic enzyme replacement therapy (PERT) in patients with pancreatic cancer and its importance to prevent weight loss, to increase survival and quality of life. They give also the comparative data in cystic fibrosis and chronic pancreatitis. I recommend only adding new median survival data which are between 20-39.5 months in patients with resectable pancreatic cancer, and 8.5-11.1 months for those with metastatic disease (References are given below). References about this topic (#55, #56 and #57) contain old information). After these small additions this review is worth publishing. References: Neoptolemos JP, et al. Lancet 2017; 389:1011-24. Von Hoff DD, et al. N Engl J Med 2013: 369:1691-703. Conroy T, et al. N Engl J Med 2011; 364:1817-25.
- 2 The manuscript by Layer and others represents a welcome contribution by providing a systematic review on the matter of QoL in PEI. The entire process is flawless, the manuscript follows guidelines for such reviews. The only thing I am missing is a flow diagram detailing the resulting publication that were analysed. I do understand, that they did not hit the studies they were looking for in the first place.

Response

We thank the reviewer for this feedback.

The information in the discussion section on page 13 has been updated according to the new references as indicated with the highlights below.

'...and median survival ranges from 23.7–39.5 months for these patients^[55] to 8.5–11.1 months for those with unresectable cancer and metastatic disease^[56, 57]'

References

- 55. Neoptolemos et al. 2017
- 56. Von Hoff *et al.* 2013
- 57. Conroy et al. 2011

We thank the reviewer for this insightful comment.

However, whilst this would be the ideal situation for a systematic review, this is not feasible for our manuscript as it is a narrative review.

Furthermore, the manuscript is under consideration as a mini-review article which are conducted in a narrative style, and do not contain study flow charts and method sections.