**Author’s response to reviews**

**Title:** Neoadjuvant chemotherapy versus surgery first for resectable pancreatic cancer (Norwegian Pancreatic Cancer Trial - 1 (NorPACT)) - Study protocol for a national, multicentre randomized controlled trial

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**Author’s response to reviews:**

Dear Editor

BMC Surgery

Thank you for reviewing our manuscript “Neoadjuvant chemotherapy versus surgery first for resectable pancreatic cancer (Norwegian Pancreatic Cancer Trial - 1 (NorPACT-1)) – Study protocol for a national multicentre randomized controlled trial”. Please find below our detailed point-by-point reply.
Reviewer 1:

1. In some cases pathological examination might reveal that the resected tumor is not optimal target for this study, such as intra-ductal papillary mucinous neoplasm or neuroendocrine neoplasms, even though the cytological confirmation was obtained before enrollment. How will you manage such cases? The author's reply of this concern was these cases would be correctly diagnosed and excluded preoperatively. I recommend that simply, you would be better to add "histological type other than ductal adenocarcinoma" to the exclusion criteria, because preoperative diagnosis is not 100%.

Answer: In the original manuscript version "resectable ductal adenocarcinoma of the pancreatic head" is an inclusion criteria. "Histological type other than ductal adenocarcinoma" has been added as an exclusion criteria.

2. When the patient with obstructive jaundice and randomized to NT group efficacy of drainage must influence and (in some cases) it might break down the randomization (Figure 1). Randomization should be performed after appropriate biliary drainage. The author disagreed on this point. I am afraid that Group 2 (Neoadjuvant) would contain less obstructive jaundice patients and Group 1 (Surgery-First) would contain more by the management drawn by Figure 1. Does this imbalance affect complication rate compared as the secondary end point?

Answer: We agree with the reviewer that Group 2 (Neoadjuvant) probably will contain less obstructive jaundice patients than Group 1 (Surgery-First) at time of surgery and that this fact can be subject to discussion. Based on a randomized controlled study from the Netherlands, we know that routine preoperative biliary drainage in patients undergoing surgery for cancer of the pancreatic head increases the rate of complications, whereas the survival rate is not affected (van der Gaag et al, New Engl J Med, 2010; Eshuis WJ et al, Ann Surg 2010). Thus, the complication rate between the groups in our study will be most probably affected by this imbalance. However, one should consider that, statistically, a small group of patients undergoing biliary drainage via ERCP or PTC will experience complications (Del Chiaro et al, JAMA Surg 2017). Thus, patients randomized to surgery-first will undergo biliary drainage only if there is a clinical indication. The imbalance in biliary drainage between the groups will be included in the data set and study analysis.
Reviewer 2:

1. I look forward to seeing the results of this very important trial. Good luck to you all.

Answer: Thank you.

With kind regards

Knut Jørgen Labori

Oslo July 26, 2017