Reviewer's report

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

Version: 1 Date: 19 Jun 2017

Reviewer: John Hoffman

Reviewer's report:

This is a very timely study and scientifically valid, except that you have added potential bias by making Time 0 from the beginning of treatment (there might be delays in either arm, probably more in SF). I would suggest Time 0 at the time of tissue diagnosis. (Obviously, marking survival from time of resection provides a lead time bias of months in favor of SF (in your secondary end points)).

2) It will be very important to record and follow ALL patients from time of entry onto the trial, as there will be those dropping out from each arm (distant metastases, toxicity, failed resection for whatever reason) and these will be of great importance and interest. Similarly, for the primary end point, you look at only those having resections. Those that fail to have resections (distant metastases, local irresectability, complications from NT) will also be of great importance.

3) The method of determining the biologic response to the NAT should be detailed, such as in Chatterjee et al. Cancer 118:3182-90, 2012. This response correlates strongly with overall survival.

4) Is there central Radiology review? This would be important to assure equality of the groups, as would initial CA19-9 values and those CA19-9 values after the completion of NAT.

5) You will receive complaints, particularly if the arms show better 1 year survival in the NAT group, that the chemo treatments are not equivalent and thus favor the NAT arm. Unless your findings are striking, another trial with exactly the same chemo arms may be in order.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

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