Reviewer’s report

Title: Standard (8 weeks) vs long (12 weeks) Timing to Minimally-Invasive Surgery after NeoAdjuvant Chemoradiotherapy for Rectal cancer: a multicenter randomized controlled parallel group trial (TiMiSNAR). Protocol paper.

Version: 0 Date: 14 May 2019

Reviewer: Bengt G. Glimelius

Reviewer's report:

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This article describes the results of an ongoing trial. First you could discuss how important and relevant this ongoing trial is? In my view it is not particularly important to explore the rates of pCR. As actually said in the manuscript, all cell killing occurs at the time of radiation and thus, any delay cannot improve the results beyond pCR. This has been repeatedly indicated in the retrospective studies and in the few randomized trials so far reported, the Lyon trial, the Turkish trial and GRECCAR-6. The Royal Marsden study, reported as an abstract, is not mentioned, but it is not published in full.

The second aspect to discuss is if this manuscript is properly written. In my view it is not. Many references are improper and the language is not stringent.

In the Background, the first reference which I haven't read describes results that are not present in any Western world environment today. Locally recurrence rates about 50% and survival rates of 30% are not seen any longer. The second sentence describes the German pre- versus postoperative trial where chemoradiotherapy was given not only chemotherapy. What about improved local recurrence rates to 7% from what? It is not proper to mix the Stockholm III trial that tested immediate surgery versus delayed surgery against the other trials that compared different time intervals, all allowing downstaging or downsizing. When giving reference to GRECCAR-6, it is stated that no impact on technical performance was seen. If I read the paper properly that was just what was reported. Further down absence of randomization but Stockholm III was a randomized trial.

It is discussed that delayed surgery may delay the start of adjuvant chemotherapy, but nothing is said in the manuscript about whether adjuvant chemotherapy should be provided or not. What actually is NOS scale? The very last sentence in the Background is not possible to understand.

Stratification is unclear. Or is it meant that substaging should be performed?
Another sentence further down at page 8 is also difficult to understand. It starts with "Due to the nature of intervention…".

When is capecitabine given, every day during the treatment or every irradiated day?

The Discussion is not much of a discussion. The whole first paragraph is a repetition of an earlier paragraph.

In the Discussion it is brought-up but that one of the goals is to determine whether MRI can be used to evaluate response, but nothing is said about that earlier.

This study will not change the current pathway of the treatment for patients with mostly intermediate and some locally advanced rectal cancers.

**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.

Unable to assess

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

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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