Reviewer’s report

Title: Study protocol of a phase II clinical trial (KSCC1501A) examining oxaliplatin+S-1 for treatment of HER2-negative advanced/recurrent gastric cancer previously untreated with chemotherapy

Version: 1 Date: 11 Feb 2017

Reviewer: Didier Meulendijks

Reviewer's report:

Dear Editor/Authors,

This study has some relevant issues.

1. the study is non-controlled and will therefore not yield definitive data on the value of the SOX 130 mg regimen.

2. the study uses ORR as the primary endpoint. ORR is notoriously poorly correlated with clinical benefit (e.g. OS, PFS), and therefore the primary endpoint will not yield relevant data.

3. the study is powered to show an ORR >45%, while other studies using SP or SOX 100 mg showed ORR rates with confidence intervals encompassing 45 (upper boundaries up to around 60). Therefore, no superiority can be demonstrated in the current study, even if it would be assumed that ORR is a relevant endpoint. Since this is a non-controlled study, no definitive conclusion can be drawn in any case (as mentioned under 1.)

In conclusion, I question whether this study is appropriately design to yield sufficient data to justify the SOX 130 mg regimen in clinical practice. I wonder whether it is ethical to perform a single-arm study that will yield minimal additional information to what is already known on the SOX regimen and which will expose patients to the risk of a higher dose of OX.
My recommendations:

1. First perform a tolerability study (phase 1), to determine the safety of the SOX 130 mg regimen.

2. If tolerability has been sufficiently investigated by the authors or otherwise, I recommend to perform a controlled study comparing safety of SOX 100 with SOX 130.

Alternatively, or even better: the authors should perform a controlled study comparing the efficacy of SOX 130 mg with the approved regimens with a clinically relevant endpoint such as OS (alternatively PFS, but OS should be feasible considering the short life expectancy of gastric cancer patients).

I hope this review helps the authors. Please feel free to contact me otherwise, and please inform me on the process of the review of this article.

best wishes,

Didier Meulendijks

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

Yes

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

No

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

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