Reviewer's report

Title: Ki67 expression and the effect of primary systemic chemotherapy on luminal breast cancer -a new concept for determining an institution-specific Ki67 cut-off value-

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Reviewer: Peter Fasching

Reviewer's report:

The authors present an article about the differentiation of chemotherapy response in luminal A like breast cancer patients using Ki-67. I have some general and some specific comments.

#1) INTRODUCTION: While I agree, that different cut-off levels for Ki-67 should be explored, the rationale presented in the introduction does not seem to meet the clinical need. There might be different cut-off levels for several therapies, while the cut-off of 14% is based purely on biological behavior. The introduction could be adjusted concerning that.

#2) INTRODUCTION/METHODS: As only immunohistochemistry was used to determine the molecular subtype it might be necessary to point out, that you mean the approximation of molecular subtype when you mention luminal (e.g. luminal like…) This is of importance as a high Ki-67 could be indicative of a basal breast cancer with positive hormone receptor status thus flawing the hypothesis of this paper.

#3) METHODS: While I support the idea, that Ki-67 should have different cut-off for different phenotypes, it is difficult to understand, why the cut-off for the differentiation between luminal A like and luminal B like tumors should be determined by the responsiveness to chemotherapy. There can be different cut-offs for all kind of phenotypes. Additionally the definition of luminal brings some more problems concerning your hypothesis (see comment #2)

#4) METHODS: The hypothesis looks like being positioned at the 50% probability in the logistic regression model to predict a pCR. This must not necessarily implicate the best cut-off for actually predicting a pCR.

#5) METHODS: How was ER positivity and how was HER2 positivity defined?

#6) METHODS: While the hypothesis is described in detail, the statistical section is missing the information, how this aim is reached.

#7) RESULTS: Please numerate the tables in the text.

#8) RESULTS: Now it seems as if ROC was used to determine the predictive value of Ki-67. The methods section should clearly describe, what was aimed at and how it was achieved.
#9) RESULTS: Please consider exact wording. The DFS can be higher or lower but a median progression free survival can be longer or shorter.

#10) DISCUSSION: There seem to be original data, which are presented in the discussion. Why not present them right away in the results section.

#11) DISCUSSION: It still does not become clear, why a cut off for Ki-67 can differentiate between luminal A and luminal B tumors.

Summarized there are several concerns with this work. The hypothesis, that a cut-off for a response to chemotherapy might differentiate between luminal A and B tumors is somewhat difficult to understand. There are completely different classification strategies for both phenotypes. However I think the study data deserves presentation, as this data is needed for current treatment strategy developments. There is a study of ours with a larger sample size in luminal tumors, that is not referred to in this study, and which might be worth mentioning (Fasching et al. BMC Cancer 2011)

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

NONE