Author's response to reviews

Title: Partial PTEN deletion is linked to poor prognosis in breast cancer

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Author's response to reviews:

Dear Professor Solera,

Please find enclosed a revised version of our manuscript entitled “Partial PTEN deletion is linked to poor prognosis in breast cancer”, which we resubmit for publication in your journal BMC.

We have now modified the manuscript according the reviewer’s suggestions as outlined in detail below.

In reply to reviewer 1

The reviewer recommends comparison of PTEN deletion with molecular subtypes of breast cancers. Moreover he request several minor essential
revisions including changes in style, removal of repetitions, improvements of English language, more details on the TMA, follow-up data, FISH probe, microscope used, statistics, wording, and figure legends.

In reply to these specific comments, we have modified the manuscript as follows:

1) We agree with the reviewer that a separate analysis including molecular subtypes of breast cancer (e.g. basal, luminal, HER2 etc. type) would be desirable. However, we have not all molecular data available on this TMA to group the tumors accordingly. We strongly believe that the core message of our work (i.e. prognostic relevance of PTEN deletion) is achieved without this analysis.

2) We used italic font for all gene names.

3) Following the reviewer suggestion we removed details on percentages and numbers of different studies from the discussion section from page 10 line 24 and page 11 line 5-6.

4) We removed repeated mentioning of “10q23” and “gold standard” from the introduction and discussion on page 5 line 21 and page 12 line 12.

5) Introduction: We have revised and shortened the introduction

6) Methodology:

1. We specified the number of TMA blocks, cores per TMA, TMA tissue core size, and numbers of samples per patient (one) on page 6 para 3.

2. We clarified the phrase “patient with and without event” on page 7 line 4.

3. We clarified that we used a home-made PTEN FISH probe on page 7 line 19.

4. We specified the microscope used for FISH evaluation on page 7 line 25.

7) Results:

1. We introduced NST abbreviation on page 8 line 24 instead of page 9 line 24.

2. We rephrased the description of the association between PTEN deletion and hormone receptor status on page 8 line 26.

3. We are grateful to the reviewer for finding the mistake related to COX proportional hazards analysis. This has not been done. We removed the respective sentence from the statistic section.

4) Discussion:

1. We added quotation marks on page 10 line 19.

2. Following the reviewer’s suggestion we have rephrased the paragraph on medullary cancers on page 11 para 3.

5) Figure section:

1. We inserted in the legend to Figure 1 that the two centromere 10 signals in
figure B and C are normal.

2. We have now clarified in the legends to figures 4 and 5 that overall survival is meant.

3. We have carefully checked Figure 5 A/B to make sure that all legends are complete.

In reply to reviewer 2

The reviewer asks for a more detailed description of the different endpoints in other PTEN studies analyzing the relationship between PTEN alterations and patient outcome. Also, the reviewer requests changes in figure labeling and presentation.

In reply to these specific comments, we have modified the manuscript as follows:

1) We specified the different study endpoints that were used in other PTEN studies in the discussion on page 12 lines 3, 8, 11, and 14.

2) We added scale bars to the images in Figure 1.

3) We changed the axis labeling in Figure 2 from amplified to amplified.

4) We represented Figure 3 as strip plots instead of boxplots.

5) We represented the Kaplan Meier plots with colored lines in Figure 4 and Figure 5.

6) We corrected NTS cancers to NST cancers page 8 line 24.

We thank the reviewers for the time and efforts dedicated to our manuscript, and are grateful for the detailed and helpful comments. We are convinced, that the valuable suggestions have lead to a marked improvement of our manuscript.

We hope that we have addressed all issues properly, and look forward to your decision on our manuscript.

With kind regards,

Ronald Simon