Author’s response to reviews

Title: Genotype-phenotype correlations among BRCA1 4153delA and 5382insC mutation carriers from Latvia

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Author’s response to reviews: see over
Dear Editor,

In this covering letter we have described the revisions performed in this version of the manuscript.

Major Comments
Reviewer: The abstract would benefit from a linguistic improvement. I struggled deciphering the meaning of the Conclusion in the abstract and still not sure if I got the meaning. This is in contrast with the main text that has a very nice flow and it is easy to read and follow.
Author: The abstract was partially rewritten and edited by a native English speaker.

Reviewer: The quality of the Kaplan-Meyer plots needs to be improved, SPSS can produce nice looking plots
Author: We corrected these figures according to the suggestions of the reviewer.

Reviewer: The table headings for Tables 2 & 3 needs a bit of clarification. Please state the endpoint, and if possible the sample size of the multivariable model. “Cox regression survival analysis of multivariate model” is not a correct formulation. Something in the style of “Multivariable Cox-regression analysis of BRCA1 mutation carrier breast cancer patients” might be better for Table 2 and something similar for Table 3.
Author: We corrected Tables 2 and 3 according to the suggestions of the reviewer. The endpoint of the multivariable model was described on page 7, line 6. The sample size was included in Tables 2 and 3.

Minor Comments
Reviewer: The description of statistical methods needs some polish, try something in the style:
“We estimated the survival function with the Kaplan–Meier estimator and calculated Cumulative incidences as one minus the survival function. Differences in survival and cumulative incidence were compared with the Log Rank test. Adjusted Hazard Ratios were estimated with Cox-regression. Association between cancer type and mutation were assessed with Odds Ratios and associated Mantel-Haenszel 95% Confidence Intervals. Comparison of two independent proportions was performed by Z-test. Statistical analysis was performed using EpiCalc 2000 version 1.02 and SPSS 19.”
Author: We corrected this description according to the suggestions of the reviewer.

Reviewer: On page 7 in the last paragraph you write “worse cancer specific survival”, it might be better to write as ‘unfavorable prognosis’
Author: We corrected this paragraph according to the suggestions of the reviewer.

Reviewer: On page 11 line 9. It would be nice if you could find a synonym for ‘mediated’. It’s nothing wrong with it; just mediation in a regression framework refers to causal inference.
Author: This paragraph has been corrected.

Reviewer: Page 11 line 18. This meaning needs some clarification.
Author: As it was suggested by the reviewer we revise the concept of this part of the discussion. The ER/PR/HER2 data were available only for a part of the patients included in the survival analysis and we are not sure that the observed differences in breast cancer histological subtypes are associated with the survival differences. In addition we found that the total size of the discussion is larger than the size of the main text and we suggested that it could be shortened. Taking into consideration all the described above, we decided to remove this part of the discussion.

Reviewer: Quality of written English: Needs some language corrections before being published.

Author: The article was edited by a native English speaker.

We would like to thank the referees for their helpful comments and hope that we have now produced a more balanced version of our article. We believe that the revised version of the manuscript is acceptable for publication.

Yours sincerely,

Grigorijs Plakhins