Author's response to reviews

Title: Genomic alterations identified by array comparative genomic hybridization as prognostic markers in tamoxifen-treated estrogen receptor-positive breast cancer

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

Thank you for giving us an opportunity to revise this manuscript. Please find enclosed the revised version entitled, “Genomic alterations identified by array comparative genomic hybridization as prognostic markers in tamoxifen-treated estrogen receptor-positive breast cancer”.

The reviewers’ comprehensive comments were very helpful and have been addressed as follows:

*Comment for quality of written English: The original manuscript had been already edited by a professional copy editing provider, English Manager Science Editing (www.sciencemanager.com).
Reviewer 1 (A. Dellas):

Comment 1: Subgroup analysis according to axillary lymph node status was added. The sample size was not sufficient especially in lymph node negative subgroup so that we couldn’t draw significant result. Only two patients had recurrence among lymph node negative subgroup. We just found several aberrations with borderline significance in lymph node positive subgroup. The detailed descriptions are in 2nd paragraph of page 13 (last paragraph of Results), 4th paragraph of page 15 (Discussion), and Table 7. The Abstract has been revised accordingly.

Comment 2: We adopted the term “invasive ductal carcinoma” in entire manuscript (1st paragraph of Methods in page 4, 2nd paragraph in page 14, and the titles of table 1 and 2).

Comment 3: The sentence was changed to “In this study, we used array CGH to assess gene copy number changes in 28 fresh-frozen ER-positive breast cancer tissue samples” in 2nd paragraph of page 4.

Comment 4: The last sentence of Discussion was changed to “An analytical tool that can identify the clones between two subject groups has not yet been established for array CGH” (Page 16).
Reviewer 2 (Pulivarthi Rao):

Comment 1: We added lists of representative genes within the amplified or lost clones in Table 3, 4, and 5.

Comment 2: Brief description about method for survival analysis with reference was provided in the last paragraph of page 10.

Comment 3: It was introduced in 2nd paragraph of page 8. “The gene copy number of one clone, BAC57_O15 (8q21.13; BAC start 82359567 and end 82463826: NCBI homo sapiens genome Build 35.1) was assayed…”

Comment 4: We have commented with references that “The majority of these regions have been reported in previous conventional or array CGH breast cancer studies” (3rd paragraph of page 11).

Comment 5: The survival comparison according to the 1p36 was added in the text without showing a figure (3rd line of page 13). It is also discussed in the 2nd paragraph of page 15.

Comment 6: The sentence was rephrased in the 1st paragraph of page 15.

Comment 7: A sentence that help interpretation of figure 3 was added to the figure legend.
Reviewer 3 (Michelle Nessling):

Major Compulsory Revisions

Comment 1: Assets of ACE algorithm were briefly described in Statistical Analysis, page 9. An introduction for SAM analysis and the explanations for parameters of SAM output were also added in page 10.

Minor Essential Revisions

Comment 1: The commercial provenience of the array used here was notified in 1st paragraph of page 6.

Comment 2: We deleted the term “high-resolution” from the entire manuscript. Representative genes located in the respective regions of gain/loss were identified and inserted in Table 3, 4, and 5.

Comment 3: We corrected the sentence as suggested (1st paragraph of page 8).

Comment 4: The exact numbers of patients in addition to the percentages were displayed in page 5.

Comment 5: Reference 14 were added to the citation list in 3rd paragraph of page 11

Comment 6: The headings of Table 1 were corrected as indicated.

Comment 7: A footnote for the “Frequency” column was added in Table 2.

Comment 8: The title of Table 3 was changed as indicated. Comment about 5q34 gain was deleted from the text, while 19p and 19q were added in the text (2nd paragraph of page 12). P-values in the Tables were corrected to “Adjusted p value”.

Comment 9: Explanations about “d” and “Fold change” were added in the Methods (2nd paragraph of page 10). It is not true that q adopts two discrete values only, but we showed only the most significant genes with those highest q values and arbitrarily cut the others with higher q values from the SAM output.
Comment 10: A point was added in front of the p value (Table 6)

Comment 11: Figure 4B was corrected as indicated.

Comment 12: Discussion was changed as suggested (the last two line of page 13 to first line
of page 14)

Comment 13: The sentences were corrected in 1st paragraph of page 15.

Comment 14: Comment about the publication by Arpino et al. was added in Discussion (the
last paragraph of page 15 to the first of page 16).

We hope you now find the manuscript acceptable for publication in *BMC Cancer*.

Sincerely yours,

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