Author's response to reviews

Title: The association between the preoperative serum levels of lipocalin-2 and matrix metalloproteinase-9 (MMP-9) and prognosis of breast cancer

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Author's response to reviews: see over
Responses to the comments on MS: 4280299458794084,

Please find our revised manuscript entitled “The association between the preoperative serum levels of lipocalin-2 and matrix metalloproteinase-9 (MMP-9) and prognosis of breast cancer” submitted for consideration for publication in *BMC Cancer*. We want to thank the reviewers for their constructive and helpful comments on our manuscript. We have responded to all comments, and feel that the manuscript is improved and has greater clarity. We have addressed each comment, in the pages below, and provide the page and lines where we have revised the manuscript. We hope that the revised version will be acceptable for publication in *BMC Cancer*.

With best wishes,

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Responses to the comments on MS: 4280299458794084:

Referee #2:

Comment 1: I am still concerned about the possible cross-reactivity of their assay. Therefore, I suggest that the authors weaken their title and change it as follows: Evidence that preoperative serum levels of lipocalin-2 and matrix metalloproteinase (MMP9) are associated..........

Response: As reviewer suggested, we changed the title from “Preoperative serum levels of lipocalin-2 and matrix metalloproteinase-9 (MMP-9) are associated with prognosis of breast cancer” to “The association between the preoperative serum levels of lipocalin-2 and matrix metalloproteinase (MMP-9) and prognosis of breast cancer”.

Referee #3:

Comment 1: In my review of this article I have continually tried to emphasize that the authors are over interpreting their findings. The history of the many many biomarker studies such as this is that the results don't reproduce in the next study. This is particularly the case when authors claim to have found interactions, such as this biomarker is particularly useful for people who have low BMI. Frankly I don't believe those results about the interactions will be found in the next study. So it is disappointing that the authors continue to talk about the interactions they have found as if it was a strong conclusion. So please remove from the final sentence of the manuscript the statement "especially in patients with low BMI and lymph node negative breast cancer."

Response: As reviewer suggested, we removed the sentence in the revised version.

[page 19, lines 2-5]
In conclusion, to our knowledge, this is the only study that has evaluated the prognostic role of preoperative serum lipocalin-2 and combined effect of lipocalin-2 and MMP-9 in patients with operable breast cancer suggesting that the elevated levels of lipocalin-2 and MMP-9 are associated with reduced breast cancer survival.
Comment 2: On page 7 it says patients were randomly selected. Was it really random, was a random number generating used? If not then the word randomly should not be used.

Response: As reviewer suggested, we removed the word ‘randomly’ in the revised version.

[page 7, lines 13-14]
After excluding the subjects with inadequate follow-up information, about 40 % (N = 370) of subjects were selected.