Reviewer's report

Title: Common genetic polymorphisms of microRNA biogenesis pathway genes and breast cancer survival

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Reviewer: Arto Mannermaa

Reviewer's report:

The manuscript "Common genetic polymorphisms of microRNA biogenesis pathway genes and breast cancer survival" represents an interesting investigation on possible association of the microRNA biogenesis pathway genes polymorphisms to survival of breast cancer patients. The topic of this manuscript is relevant; the role of microRNA’s biogenesis pathway genes in cancer development and progression has been well established but the association between genetic variants of this pathway genes and breast cancer survival is up till now unknown.

The authors have chosen to focus on 41 functional SNPs on 13 genes. The material used is well characterized though moderate in size and especially so in the number of patients with a relapse or who have died. Authors do not present power estimates to detect significant ORs. Presumably the authors have been confident with this and have decided to implement the project. The genotyping methods used are valid and properly described. However the choice of SNPs and power analysis need more clarification.

This manuscript describes evidence for microRNA biogenesis pathway gene variants to have an effect to breast cancer patient survival. The paper is mostly concisely and very clearly written, and with pretty convincing considering the obvious lack of power. The other major weakness of the manuscript is in the description of the statistical analyses. It is now unclear what is the final model authors have used in Cox's regression model? What is the reason to omit menopausal status, lymph-node status, distal organ metastasis, ER status, PR status, Her2 status, histological grade, adjuvant chemotherapy, endocrine therapy, and radiotherapy as covariates? At least a supplementary table should be included to show the effect of these on HR. It is also not clear why breast cancer specific survival was not used. How many of 41 deaths were due to breast cancer?

The manuscript has some points to revise before it is acceptable for BMC cancer

1. Power analysis: The authors have not utilized a power analysis to prove the size of the material and selection of SNPs to be appropriate for the analysis. This
should be included.

2. In the summary the authors suggest further studies with larger sample sets. Also discussion concerning full microRNA genes and binding sites and their genetic variants should be engaged.

3. In description of the study population there is something obscure: “Patients were followed from October 2009 to March 2010 using a retrospective chart review with standard protocol to collect clinicopathological features, patients’ treatments, and vital status such as recurrence and death. Patients were diagnosed with in situ breast cancer (n = 49), benign breast cancer (n = 13), or multiple cancer at diagnosis (n = 2).” How were the rest of patients diagnosed, how many were excluded by the incomplete record data linkage?

4. Include the effect of all clinicopathological covariates on HR at least as a table. For Cox regression analysis major covariates could be used, i.e. age, tumor size, lymph node status, grade, and ER-status.

5. The authors should discuss on the effect of the studied polymorphisms on non-Asian populations as the minor allele frequencies may vary considerably.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests