Reviewer’s report

Title: Histone demethylase GASC1 - a novel prognostic and predictive marker in invasive breast cancer.

Version: 1 Date: 25 July 2012

Reviewer: Anna Sapino

Reviewer’s report:

The article describes the possible role of Histone demethylase GASC1 as a new prognostic and predictive marker in breast cancer. It deals with a relevant issue, but some elements preclude the acceptance of the paper in the present form.

Major revisions

1. Background This introduction does not emphasize enough the significance of the marker presented in the study. We suggest the authors to better underline the study purpose and the hypothetical central role of GASC1.

2. Material and Methods The criteria used for the selection of the cases are not shown. In the Immunohistochemistry section the authors say: “After initial standard procedures the sections were incubated overnight at 4°C…” but the procedures are not described. Both positive and negative controls are lacking. The cut-off value for GASC1 positivity is absent. The authors illustrate the kit for mRNA analysis but they do not specify if the reaction has been performed following the manufacturer’s instruction or a specific protocol.

Reference (endogenous control) genes should be more than one.

3. Results “From the total material (392 tumors) we excluded 37 benign and in situ cases”. This means that the study has been conducted on 355 specimens.

Section: “GASC1 negativity is an independent prognostic factor of worse breast cancer specific survival.”

Section: “GASC1 negative cases are more likely to have a relapse of breast cancer and to suffer from more aggressive tumors than the GASC1 positive cases”

It is not clear which is the difference in the two paragraphs

The term “MORE” has to be cancelled and substituted with numbers.

Section: “GASC1 mRNA expression is in line with the immunohistochemical data.”

Please state the value used to define low/high expression of GASC1mRNA.

“In contrast, HER2 negative cases showed significantly higher GASC1 mRNA expression than HER2 negative ones (Mann-Whitney: p=0.004) which was in line with the protein staining results”: “negative” is repeated two times and the sentence has no meanings.
Discussion “An interesting finding from the survival analysis was that HER2 negative patients survived significantly better when they had GASC1 positive tumors regardless of their clinical stage. This observation might open new therapeutic possibilities, especially for the patients with triple negative tumors”. Why? The relationship with the AR is not clear.

Conclusion “Evaluation of the GASC1 status could enable more accurate qualification of patients for adjuvant therapy”. Why?

Minor revisions

Abstract is not organized properly. The aim of the work is missing. The Background section contains some Material and Methods. In the sentence “In our material 56% cases were GASC1 negative and 44% positive” the authors have to state the method used to obtain these results. Please substitute the expression “more” (i.e. Among GASC1 negative tumors there were more estrogen and progesterone receptor negative cases and more HER2 positive cases than among GASC1 positive one) with an appropriate scientific terminology.

Figure 1: The IHC figure shows an intense background. Where should the IHC-staining be located? “Positive immunostaining in nuclei of epithelial cells (immunoscores: 3 for the nuclear number and 3 for intensity of nuclear staining), positive staining also visible in cytoplasm.”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have No conflicts