Reviewer's report

Title: HTF9C expression is prognostic in her2+ breast cancer

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Reviewer: Peter Sinn

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The authors have analyzed a cohort of 69 HER2 positive breast cancers for multiple markers in the search of markers that can be used for prognostic subclassification. This approach is very relevant, because currently there is no way to define prognostically adverse subgroups within the HER2 class. The methods have been described in sufficient detail, but apparently immunohistochemistry was performed manually which is not state of the art and may contribute to considerable variation to the staining results. But, as this is an outcome study, the statistical methods should have been made clear. This is totally missing, as there is no information given as to the kind of statistics used, the median follow-up period of the patients, the amount of missing information, what was regarded as recurrence (local? distant?) etc. Contralateral breast cancer cannot be regarded as recurrence. In nearly all cases this is a new disease.

This is a HER2 patient cohort that did not receive adjuvant Trastuzumab. Therefore, tumor recurrences are not related to Trastuzumab resistance but reflect the natural course of HER2 positive disease. However, in the western world Trastuzumab now is standard for the adjuvant treatment of HER2 breast cancer patients, and therefore these data cannot be extrapolated to patients who received Trastuzumab treatment. The authors conclude that „HER2+/HTF9C+ breast cancers are more likely to recur treated with traditional cytotoxic therapy alone” but this is not justified because response to Trastuzumab therapy is not known and not all but only „some“ patients have received cytotoxic chemotherapy. These limitations are not discussed at all.

It is suggested to reanalyze the data with a better definition of tumor recurrence and to analyze the effect of the cytotoxic therapy that was actually given to the patients or not in the knowledge of the antigen expression of this marker.

Level of interest: An article of limited interest

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