Reviewer's report

Title: HTF9C expression is prognostic in her2+ breast cancer

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Reviewer: Arndt Hartmann

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Major compulsory revisions

This is an interesting report investigating the expression of HTF9C in Her2+ breast cancer. The authors identified HTF9C as a up-regulated marker of poor prognosis in Her2+ breast cancer cases in a large-scale screen of antisera. The overexpression was confirmed in three independent cohorts, each with 60 to 80 cases of Her2-positive breast cancer.

The results are very promising and point to a candidate marker which could detect high risk Her2+ patients.

Although the paper is well written, there are several points which have to be addressed before the manuscript can be published:

1. It is not entirely clear how the authors defined Her2 positivity. In the RPCI cohort they report that all cases have been detected by immunohistochemistry using the Hercep-Test with the result of 3+. In contrast there are no data indicating the methods to detect Her2 in the CCIH and CCF datasets. Because the authors have a tissue microarray in their hand they should repeat the immunohistochemical staining for all three cohorts and in addition investigate the amplification of Her2 using FISH. These data are absolutely essential because Her2 determination within the described cohorts are not reported according to the guidelines used for daily diagnosis.

2. The authors report univariate and bivariate analysis. A multivariate analysis should be done.

3. Two different antibodies were used in the study. For both antibodies no data are reported for the specificity of the staining. The authors should report Western blots which clearly show the specific staining with the used antibodies and in addition should perform blocking experiments using the specific peptides. Because the authors propose this marker as a clinical diagnostic test I think this is also essential for determining the usefulness of this antibody for clinical purposes.

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.