Reviewer's report

**Title:** Differential survival following trastuzumab treatment based on quantitative HER2 expression and HER2 homodimers in a clinic-based cohort of patients with metastatic breast cancer.

**Version:** 1  **Date:** 2 June 2009

**Reviewer:** Reiki Nishimura

**Reviewer's report:**

The authors stated that higher HER2 levels predicted better survival outcomes following trastuzumab treatment in the high HER2-expressing group using HERmark to measure HER2 expression and HER2 homodimers. It is difficult to say that trastuzumab can prolong the survival time in this study. In the background section of the abstract, the authors mentioned that response rate and time to progression are important to explore the predictive marker for trastuzumab therapy. Therefore, in order to evaluate the efficacy of trastuzumab, the response rate and time to progression are needed for this study. However, this study is somewhat interesting.

1. The authors should explain the methods of immunohistochemical evaluation for ER, PgR, and HER2 in detail as well as the criteria for the positivity of ER and PgR. They evaluated immunohistochemical values of HER2 expression and approximately one-third of the specimens were scored as 0 or 1+ upon repeat testing. Therefore the methods of immunohistochemical analysis are important.

2. Trastuzumab treatment is recommended for patients with IHC: 3+ or FISH+. Are there any patients treated with trastuzumab for HER2: 2+ tumors?

3. The authors should show the numbers of patients, patients' characteristics and the IHC score according to the H2T subgroup. What are the relationships between low HER2-expressing (< the median value of H2T) sub-groups and low HER2 score on repeat testing? The patients that had tumors with IHC: 0 or 1+ are not candidates for this treatment.

4. We would like to know the relationship between OS and IHC score on repeat testing.

5. The authors should show the results of univariate analysis of the factors such as tumor size, nodal status, ER, and the number of metastatic sites.

6. In Table 1, there was duplicate information for ER+PR-. This should be made clearer.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being
published

**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.