Reviewer's report

Title: Connexin 26 and 46 expression refines intermediate prognostic subgroups of residual tumor classifications in neoadjuvant treated breast cancers

Version: 1 Date: 17 July 2012

Reviewer: A Jager

Reviewer's report:

Teleki et al have investigated the prognostic role of connexin expression in neoadjuvant treated breast cancer patients. It is a relevant and well defined research question from a pathophysiological as well as clinical point of view. The study is well designed and the paper is clearly written.

A major comment

From the literature it is already known that pre-treatment TNM classification, receptor status as well as post-treatment pathological response data are all independent predictors of long term outcome (survival). Since connexin expression levels are described to be correlated with TNM parameters or receptor status by the authors, it should be excluded that connexin is just a surrogate measure of one of these variables (TNM parameters or receptor status). The authors should perform multivariate analyses (Cox proportional-hazard regression; corrected for at least relevant TNM parameters or receptor status) to confirm the independent association of connexin Cx46/Cx26 with survival.

Some minor comments

The authors aim to correlate connexin expression and cell proliferation with clinicopathological parameters. Although these results are more or less described in the results section (page 8), an additional Table with all detailed information about these correlations should be added.

In general, Ki67 is used as a score (or index) expressing the percentage of positively staining cells among the total number of invasive cells in the area scored, often defined as a dichotomized variable of high and low expression. The authors have used a 0-10 scale. Could the authors please describe the quantification of the Ki67 they have used in more detail? Could they also substantiate the choice of the 0-10 scale by providing references and data validating the use of this scale? Finally, it would be informative to add the information on Ki67 scores to Table 1.

In Figure 5, in contrast to the other 5 graphs, in the lower right graph the subgroups are divided in 0 vs. +1,+2 and +3. Consistency is advisable, so please change these division in 0 and +1 vs. +2 and+3.
A paragraph mentioning the limitations of this study should be added to the discussion section.

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

**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'