Reviewer's report

Title: Estrogen receptor beta as a predictor of endocrine therapy responsiveness - a randomized neoadjuvant trial comparison between anastrozole and tamoxifen for the treatment of postmenopausal breast cancer

Version: 1 Date: 15 May 2013

Reviewer: Tesa Severson

Reviewer's report:

Major Compulsory Revisions:

1. Title: The title currently is misleading. The data support ER# along with ER# can predict response to endocrine therapy. The title needs to be altered to reflect the predictive power of the ER#/ER# ratio, rather than ER# alone.

2. Page 11, paragraph 1: The use of the Allred score for determination of IHC staining should be defended with a figure showing IHC assays are not over saturated. Otherwise, use the proportion of cells staining positive.

3. Page 13, paragraph 1: Since the claim is that more information can be gained with the addition of ER# staining, ER# data needs to be for added comparison.

4. Page 13, paragraph 2: Only 57 of 78 cases were ER# positive. In a clinical situation these patients would not typically be treated with endocrine therapy. Comment on these patients and their inclusion in the study.

5. Page 13, paragraph 2: The title of the study is “Estrogen receptor beta as a predictor of endocrine therapy responsiveness – a randomized neoadjuvant trial comparison between anastrozole and tamoxifen for the treatment of postmenopausal breast cancer”. To conclude that ER# is a predictor of endocrine therapy response when the group, which is ER# positive and ER# negative, is too small for statistical analysis is premature. In fact, those patients with a ratio <1 of ER#/# (page 14, paragraph 1) were not significantly different in their Ki67 levels suggesting there may be little prediction value for endocrine therapy response in ER# only cases. I suggest changing the title of the paper to reflect the importance of the ratio of ER#/ER# or examine more ER# positive/ER# negative patients or retrospective assessment of ER# from other trials to determine the validity of the current title.

6. Comment on the dose of tamoxifen, is 20mg/day enough without a loading dose to reach steady state in 26 days? In addition, these patients are compared with patients treated with AIs which reach steady state levels much faster than tamoxifen. Is there a bias in the data because of this? (Soininen et al. J. Int. Med. Res. 1986 and Buzdar Clin. Can. Res. 2003) Measurements from the plasma of patients showing therapeutic levels of tamoxifen after treatment would be useful.

7. Add a section where limitations of the work are clearly stated.

Minor Essential Revisions
1. Page 1, paragraph 2, sentence 2: remove “final”.
2. Page 1, paragraph 2, sentence 3: remove “to”.
3. Page 6, paragraph 2, sentence 1 and 2: references required.
4. Page 9, paragraph 1, sentence 1: What is the range for data described?
5. Page 11, paragraph 1: Kappa value for IHC scoring from different pathologists.
6. Page 11, paragraph 4, sentence 1: replace “was” with “were”.
7. Page 14, paragraph 3, sentence 2: replace “prognosis” with “prognoses”.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.