**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:** 18 May 2013

**Reviewer:** Etienne Leygue

**Reviewer's report:**

**Major comments**

The authors did not mention the existence of variant forms of ER beta that are however clearly expressed in Breast cancer; mainly ER beta 2 or Cx (see: Estrogen Receptor # (ER#) Level but Not Its ER#cx Variant Helps to Predict Tamoxifen Resistance in Breast Cancer, Majida Esslimani-Sahla et al. Clin Cancer Res September 1, 2004). For the latest on ER beta variants see Endocr Relat Cancer March 26, 2013 ERC-12-0389 and references herein. Because it seems that the antibody used (14C8 from Gene Tex, raised against 1-153) recognizes all the different ER beta isoforms without discrimination, any result should be analyzed and presented with this major consideration in mind.

Figures should be added to present detailed example of staining for each antibodies, to illustrate cases considered positive and negative for ER beta and alpha, and show examples of ratio<1, between 1 and 1.5 and >1.5

Legend of Figure 3 is far too incomplete and this figure is potentially not called in the result section.

The authors said they calculated the "ratio" ER alpha/ER beta: what was then done when ER beta score was zero?

Many important details are missing: how many cases belong to the ratios classes defined, how many exactly are negative for ER alpha in the different categories etc... additional Table could solve this issue.

**Minor issues**

Recent review on ER beta should be included.

The author could mention and discuss Yan Y. Ann Oncol. 2013 Apr 11. [Epub ahead of print]

In Table 2, it seems that KI67 is lower in ER beta negative used in placebo (mean and median) than in anastrozole and tamoxifen? could that not affect the variation? this should be addressed.

In this table, the sum of anastrozole post treatment is 24 patients... should not it
be 25 according to table 1?

Page 18, change of ratio alpha/beta during breast tumorigenesis was first shown by Leygue et al 1998, Cancer research 58, 3197 not ref 12.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare I have no competing interest