Reviewer's report

Title: Interrogating differences in expression of targeted gene sets to predict breast cancer outcome

Version: 1 Date: 30 December 2012

Reviewer: Sunil Badve

Reviewer's report:

Major revisions:
1) The authors provide a detailed bio-informatic analysis of the gene expression including multivariable analysis. However, one issue that always comes up is the role of tumor grade. All the molecular signatures generated to date show that this is an important parameter; thus analysis of grade needs to be performed to document the relative superiority of the gene signature.

2) In this day and age, considering breast cancer as a single disease and excluding parameters such as age, tumor size and nodal status which form the basis of clinical decision making is asking for trouble. These need to be included in multivariable analysis of any new prognostic/predictive markers in breast cancer.

3) It is not clear from the paper whether the signature works as efficiently in both ER+ and ER- disease. Clarifications are needed. This is pertinent since a number of genes within the signature are ER regulated. The efficacy in ER- subset needs to be demonstrated.

Minor:
I will defer to the experts for opinion on the bio-informatics analysis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
Nil