Reviewer's report

Title: Multivariable regression analysis of febrile neutropenia occurrence in early breast cancer patients receiving chemotherapy assessing patient-related, chemotherapy-related and genetic risk factors

Version: 2
Date: 18 December 2013
Reviewer: George Dranitsaris

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The major points that need to be addressed are:

1. The FEC regimen is not used very much in the modern era. Therefore the clinical relevant of a model based on a substantial number of patients who received FEC is questionnaire.

2. In many centers, the genetic data is not routinely collected. Therefore how practical is it to include such data in a risk prediction model.

3. The models for FEC and FEC-D were combined. Instead, two separate models should have been created. If not, then type of chemo should have been in the model as a predictor variable.

4. It is stated that all patients included in the study gave written informed consent. But is is stated in the paper that the data was collected retrospectively?

5. Page 5; you need to state the definition of febrile neutropenia

6. There are major issues in the statistical analysis. For example, the authors did not adjust for clustering on treatment cycle, they did not do model calibration, nor did they do internal validation using methods such a boot strapping.

7. Some patients received up front G-CSF with their chemo. Use of primary G-CSF was not added as a risk reduction variable in the model. This needs to be at least tested for.

8. In table 3, the docetaxel part of FEC-D was not tested as a stand alone variable. This is the main cause of febrile neutropenia with this regimen.

9. In table 3, the coefficients need to be reported as odds ratios.

10. The risk of febrile neutropenia is not linear. None linearity of risk by cycle of chemo not tested in the model. It needs to be,

11. Overall, both of the models have a very poor predictive ability, as indicated by the low area under the ROC curve. At a minimum, the ROC should be 0.7.

Level of interest: An article of insufficient interest to warrant publication in a
scientific/medical journal

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

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

**Declaration of competing interests:**

none