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: 20 December 2013

Reviewer: Victoria Chia

Reviewer's report:

Major compulsory revisions

1) Background, 5th paragraph - the authors mention a risk model they conducted for FN in NHL patients, but that the model performance was decreased and that more refined models are needed. How is this relevant to the breast cancer patients and why is this important for this study?

2) Background, 5th paragraph - the authors also discuss that including genetic factors may increase prediction of FN risk. Can the authors please expand why they think this may be true?

3) Methods, study population – although the authors cite their paper on the selection of the SNPs, it would be good to add a brief section in this paper on the reasoning of the SNPs, as it may not always be possible for readers to have access to the text of the other paper.

4) Results, Table 3 – in the SNP section, what is the p-value testing in the first row for each of the SNPs (e.g. MRP1rs4148350 (GG reference) has a p-value of 0.000)?

5) Results, Table 3 – why are variables with p>0.25 included in this table if 0.25 was the cut-off for inclusion in the multivariable model?

6) Results and Table 4 – The TT estimate for MRP1rs4148350 is likely to be unstable as there are only 5 patients in that category and more variables than patients being included in the model. It would be a stretch to say that carriers of the T allele predicts FN risk given this and that the heterozygous group does not show a statistically significant increased risk.

7) Discussion – it is concerning that known risk factors for FN, such as age, were not shown to be predictors in this model and that the model could not be validated. Given these limitations, the validity and usefulness of this model is questionable and definitely does not warrant the strong conclusion statements.

Minor essential revisions

1) Methods, study population – please define “early” breast cancer.

2) Methods, descriptive and univariable analysis – please explain why p#0.25 was chosen as a cut-off for inclusion into the multivariable model.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Yes, I am an employee and shareholder of Amgen Inc