Author's response to reviews

Title: The use of chemotherapy regimens carrying a moderate or high risk of febrile neutropenia and the corresponding management of febrile neutropenia: an expert survey in breast cancer and non-Hodgkin’s lymphoma

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Author's response to reviews: see over
Dear Editor,

The manuscript entitled “The use of chemotherapy regimens carrying a moderate-to-high risk of febrile neutropenia and the corresponding management of febrile neutropenia: an expert survey in breast cancer and non-Hodgkin’s lymphoma” was revised following the comments received from BMC Cancer editorial on September 13th. A point by point reply to each reviewers’ comment is available hereafter. All changes in the manuscript compared to the submitted version were done using track changes, references were re-ordered following the insertion of new quotes. Reviewers’ comments as well as the revised version of the manuscript were circulated to all co-authors for review, and final approval were obtained.

We would like to thank the reviewers Ruth Pettengell and David Henry for the careful appraisal of the paper, and hope that our answers and edits are addressing their comments in a satisfactory manner.

With best regards,

Laetitia.
**Reviewer: Ruth Pettengell**

Major Revisions:

1) Belgium has participated both in European retrospective and prospective studies of FN in both breast cancer and NHL (Papers referenced and also in Bosly et al 2008 Ann Hematol and Doorduijn JK et al. Blood 96:133a (abstract 575). Some of these papers are already listed in the references. This audit data should be discussed in the clinical context of this previous work in Belgium and Europe in the discussion.

Discussion was amended accordingly, using the above-mentioned references plus other publications. In general, we try now to compare (as far as possible) our results on different levels: incidence of FN, protective effect of G-CSF (FN and dose-intensity), and disease burden. This was indeed overlooked in the submitted version, or at least the link to existing studies was not clearly established.

All inaccurate broad spectrum statement such as in the background must be removed.

See deleted sentences in introduction, quantitative results were added wherever possible.

That the data is retrospective covering a 6 month period should be detailed in the abstract.

OK, done

Was any attempt made to analyses patient comorbidities, or individual risk factors to help define risk or explain the high FN rates.

Unfortunately, there was no possibility to collect such data on top of the chemo regimens info and FN/PSN occurrence, given the design of the study.
(investigators retrieving info themselves) and the objectives (high-level description only).

The use of the term of moderate to high risk is misleading and should be amended to moderate and high risk regimens.

OK, done.

For Health commissioners to change practice and fund primary prophylaxis for these patients there must have been some more detailed Health economic data or cost analysis performed. It would be of interest to include this.

In the full report submitted for obtaining extra reimbursement, both stronger clinical evidence (meta-analysis Kuderer et al 2007) and budget impact considerations were indeed provided, on top of the survey data.

Kuderer data is now presented in the introduction, whereas budget impact estimation is confidential data (thus no possibility to add it to our paper).

For information, a summary of the rational for granting the extension of reimbursement of Neulasta can be found here (only available in Dutch):


The discussion needs to rewritten in the context of the literature and not just repeat the results.

The HOVON and INC-EU studies are now presented more in depth in the discussion, especially what can be compared with our findings, and what cannot.

Results summary/reminder of our results was made shorter.

Minor Revisions:
P 11 the last sentence of 'G-CSF in FN prophylaxis (BCC) is unclear, also the paragraph on 'real life recurrence' is unclear.

The corresponding section was rephrased.

What does 'cycle suppression' mean?

Cycle not done (skipped) – changed in the text as 'dropped cycles'

**Reviewer: David H Henry**

Reviewer's report:

The strength of the study is that the FN risk in breast cancer patients in the first cycle was 31% and 48% in NHL patients, much higher than reported in clinical trials using these regimens in these patients.

You also point out that the downstream consequences of FN without prophylactic growth factor are quite significant requiring more and longer hospitalizations and IV antibiotics, which is also quite important.

The negative aspects of the study are that it is a small sample size and retrospective and that the number of tables and charts is way too many. There is a wealth of data here, but the retrospective small sample could introduce significant bias and to give so much detail leads to a “torturing” of the data.

Your conclusions are reasonable given the fact that you mention the potential for bias with the relatively small sample size.

**You should consider significant reduction in numbers of tables and charts which a relatively too many given this small sample size.**

The number of tables was cut from 7 to 4, with minimum loss of information:
Table 2 (Breast cancer) and Table 5 (NHL) were deleted. Information about the different chemo regimens and number of patients was added as footnotes of Table 1 (breast cancer) and previous Table 4 (NHL), now Table 2. Tables 3 and 6 were merged into a single table (now Table 3), showing mainly the results over all chemotherapy regimens, plus detail for the 2 most frequent breast cancer regimens and dose-dense regimens in NHL. Table 7 about expert opinion remains unchanged (now Table 4).