Author's response to reviews

Title: Cost-effectiveness of a 21-gene recurrence score assay versus Canadian clinical practice in women with early-stage estrogen- or progesterone-receptor-positive, axillary lymph-node negative breast cancer.

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Author's response to reviews: see over
To the Reviewers,

We would like to thank the reviewers for reading and commenting on our submission to BMC Cancer entitled "Cost-effectiveness of a 21-gene recurrence score assay versus Canadian clinical practice in women with early-stage estrogen- or progesterone-receptor-positive, axillary lymph-node negative breast cancer". We are pleased to resubmit a revised version of our manuscript after considering the reviewers’ comments. We have provided a point by point summary of the changes that we considered based on the reviewers comments:

1. Reviewer’s comment: “Add that use in provinces with reimbursement mechanisms likely increasing and field evaluations in these centres would be helpful to establish impact on practice; a few of these are ongoing in Ontario.”

Response to reviewer: we have added the following text on page 5 “However, the use of the test with reimbursement mechanisms is likely increasing”. We have also added the following text on page 6 “but few field evaluations to establish its impact on Canadian practice are ongoing in British Colombia and Ontario”.

2. Reviewer’s comment: “Mention more explictly that newer third generation anthracycline-taxane regimens have different costs and slightly better efficacy so analysis with such data would be more applicable to current pratice landscape”.

Response to reviewer: we have used the following text on page 17 “Newer third generation anthracycline-taxane regimens have different costs and slightly better efficacy so analysis with such data would be more applicable to the current practice landscape” in place of our previous statement “outcomes of therapies given in the 2000-2002 population may not necessarily reflect the possible benefits of other types of adjuvant therapies or dosing schedules used in current practice”.

3. Reviewer’s comment: “There is at least one other evaluation of RS-assay in a Canadian setting that should be incorporated (Lamond et al, Breast Cancer Research & Treatment 2012)”.

Response to reviewer: we have incorporated Lamond et al analysis in our discussion on page 6 and 15. We have referenced this analysis on page 6. In addition, we have revised our statement on page 15 as follows: “Two recent studies were conducted from the Canadian health care payer’s perspective; however, the first analysis did not address all the limitations mentioned above, and modeling the current experience of ER+/ PR+ LN-ESBC population with regard to survival in both analyses was not based on Canadian data and real world clinical practice. In all studies there was no differentiation in adjuvant chemotherapy practice between pre- and post-menopausal women as recommended by Canadian guidelines, whereas we observed differences in clinical practice for these two groups (Table 2).”
4. Reviewer’s comment: “In the sensitivity analysis, the phrasing "the RS-assay generated negative incremental cost and effect..." is unclear. Was incremental cost negative (good), incremental effect negative (bad), or both (ambiguous)? Table 4 ......does not help clarify this point”.

Response to reviewer: we have explained the term "the RS-assay generated negative incremental cost and effect..." by adding the following text in a bracket on page 14“(the RS-assay led to decrease in both cost and effect)”.