Reviewer’s report

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.

Version: 2 Date: 27 May 2012

Reviewer: Doug Coyle

Reviewer’s report:

Major compulsory revisions.

1. In the original review the first compulsory revision requested was as follows:

“When evaluating a test the usual focus is on the sensitivity and specificity of the test. Thus, in this context the test (or CCP classification) is evaluated based on the ability to assign chemotherapy to the correct patients. The proportion of patients who are high, intermediate and low risk will be the same in both tests – the issue is that there will be differential rates of misclassification between these tests and therefore different degrees of “inappropriate” use of chemotherapy. The current standard does not take this approach. Rather it takes two separate cohorts of patients, one using the risk classification and the other using the assay and determines the patients risk and use of chemotherapy specific to these cohorts. The major concern is, are the cohorts truly comparable as any difference between these will lead to bias in the estimates of cost effectiveness.

An alternate approach would be to take the data from B-14 and B-20 and compare the risk stratification if we had applied the CCP classification as well as the RS assay. The analysis could then focus on the use of chemotherapy within these cohorts as defined by the RS assay. Survival curves could then be applied stratified by risk and chemotherapy use from the B-14 and B-20 trials. This would allow the two strategies to be compared using the same dataset.”

The authors have recognized that this would be the desired approach. However, they have not yet been able to convince me that the approach adopted avoids the possible biases that may occur when deriving transition probabilities for two alternate treatment strategies from two disparate data sources. This needs to be addressed more fully in any revised manuscript. The analysis hinges on the comment in the response to reviewers “Note that we had enough patient, clinical and treatment data from the Manitoba Cancer Registry to make our study cohort comparable to the populations targeted in B-14 and B-20 (hormone receptor positive, lymph node negative, and early stage breast cancer (stage I and II)).” I’m not convinced that the authors have fully proved this point.

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:

No conflicts to declare