Reviewer’s report

Title: Cost-effectiveness analysis of the introduction of S-1 therapy for first-line metastatic breast cancer treatment in Japan: results from the randomized phase III SELECT BC trial

Version: 0 Date: 13 Aug 2017

Reviewer: Rei Goto

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In this paper, the authors perform a full economic analysis of chemotherapy for metastatic breast cancer in Japanese settings. They compared two regimens based on a published P3 trial (SELECT), in which cost and QALY data are taken, and showed that oral S-1 therapy is highly cost-effective, more so than taxanes. Overall, this paper is well-structured and presents results clearly. I admit that this is a good paper. However, there are some comments and suggestions as below.


2. In this analysis, HRQOL data and cost data are acquired from about half and a quarter of the samples in the trial. As the authors admit, it is important to analyze whether selection biases, if any, can have impacts on results or not. It is hard to conclude about this without further statistical tests on the differences in baseline characteristics among trial, QOL and cost samples. Detailed analysis is needed to confirm the authors’ assertions.

3. The authors need to give more details about how they calculated expected QALY. How did you cope with missing QOL data (score level and/or item level)? Did you replace missing fields with estimates? Without replacing, how did you treat this unbalanced panel data?

4. Linear mixed models for repeated measures could be explained more carefully. Showing estimation results in the Appendix is helpful to see the impact of each variable.

5. How is QALY, after the final visit, computed? It is better to explain the computations of QALYs separately before then.

6. The expected calculation of cost also needs more explanation. How did you connect the Kaplan-Meier data to cost data? How about the length of the intervals? How did you estimate the average cost over the interval? Did you use any leased square methods or others? If so, presenting estimation results in the Appendix would be helpful.

7. Do patients in this trial tend to receive terminal care in the same institution? If not, it becomes very difficult to assess the potentially big resources used in this phase. Please discuss this issue.
8. Can oral agents like TS-1 reduce the frequency of outpatient visits? If so, time cost of patients and families can be reduced. Please discuss this even if the authors focus on the public healthcare perspective.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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