Author's response to reviews

Title: Comparative benefit from small tumour size and adjuvant chemotherapy: clues for explaining breast cancer mortality decline

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Version: 5 Date: 23 July 2014

Author's response to reviews: see over
Dear Dr. Thomas Ruhstaller

Journal Editorial Office - BioMed Central

The manuscript **Comparative benefit from small tumour size and adjuvant chemotherapy: clues for explaining breast cancer mortality decline** has been revised according to the points raised by reviewers.

We acknowledge the high quality of the reviewer comments that allowed important improvements for the manuscript.

Reviewer 1

All arguments were approached by 1) modifying a sentence in the Introduction section (page 4); 2) adding to the Discussion section a specific paragraph (page 12) and a sentence to the last paragraph (page 13). Accordingly, four references were added as well.

Reviewer 2

- The question regarding node-negative patients is addressed in the Discussion section (page 11).
- As requested, the cumulative incidence function were added (Figure 1, page 7)
- Legends of Figures 2 and 3 (formerly figures 1 and 2) were changed as requested and all absolute risk reductions in figures were reported as positive values.
- In the Introduction section the possible effects of mammographic screening have been re-stated by mortality reduction instead of survival improvement.
- The reason for the apparently discordant results in comparison with Bonadonna et al. reports, which were noted by the reviewer in tables 1 and 2, lies in the use of a different measure of disease occurrence and association. Actually, we repeated the analysis of Bonadonna et al. with the non-parametric estimator for competing risks and, in fact, the effect resulted significant ($p=0.002$, unadjusted). However, in the tables, we report the probabilities of recurrence (using differences as a measure of effect) and not the sub distribution hazards (using ratios as a measure of effect). Therefore, we cannot expect that the confidence intervals of probabilities of recurrence be without overlap during the whole follow-up. In our analysis we adopted ARR, which is expected to be less efficient but more informative than the hazard ratio to understand the impact of the considered factors through follow-up time. We believe that this point would be redundant in the text and suggest maintaining it as explanation for the reviewer only.

Finally, the Editor’s suggestion has been followed (page 12).

All changes are detectable using track-changes in the re-submitted manuscript.

Best regards.

Romano Demicheli.

Federico Ambrogi.