Author’s response to reviews

Title: Adjuvant Trastuzumab in the Treatment of HER-2-Positive Early Breast Cancer: A meta-analyses of published randomized trials.

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Dear reviewer: Andrew Roddam

We are grateful regard your attention to our manuscript. We understand the real importance of the suggested corrections and we reviewed that manuscript following all the recommendations. The major compulsory revision was totally followed.

1. The authors continue to present the result of a fixed effects analysis for cardiotoxicity even though there is heterogeneity. They also claim that the insignificant result for a random effects model is insignificant. Given that this p=0.07 and heterogeneity tests are known to be underpowered this is still suggestive that there is residual heterogeneity between studies. My recommendation is therefore not to present a single estimate but to say that there was considerable heterogeneity and the overall results are dominated by one single study which renders the meta-analysis quite uninformative. They can of course say that it would appear that there is an increase in cardiac risk associated with HER2 (as I recommended in my previous review). 2. There are still places in the results section (and elsewhere in the manuscript) where the English does not make sense and it is difficult to assess the point the authors are trying to make.

We follow exactly the recommendations. Thus, we have introduced a flowcart according to QUOROM criteria and it did the correction of the English mistakes present in the manuscript. In the discussion section, we considered that there was considerable heterogeneity between studies regarding cardiotoxicity as suggested by reviewer. We also introduced in the results one analyses on publication bias and one graphic called "funnel plot", according to QUOROM guidelines.

We would appreciate if you could publish our analysis
Gustavo Viani, first author of that article.