Author’s response to reviews

Title: Trastuzumab with either docetaxel or vinorelbine as first-line treatment for patients with HER2-positive advanced breast cancer: a retrospective comparison

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Author’s response to reviews: see over
Candiolo, 23/DEC/2009

Dear Sir or Madam, thank you very much for giving us the opportunity to submit a second revised version of MS # 1525853606286982.

We have valued all the concerns raised by the referees and the manuscript has undergone the minor revisions requested by referees number 1 and two. Furthermore, we have also addressed the concerns of referee number 3 although the two main revisions suggested have been already addressed in the first revision of the manuscript, as requested by referees 1 and 2.

We hope that in its current format the paper will now be suitable for final acceptance.

Referee 1:
All the suggested corrections have been considered and included in the present version. p5, line 14 has been rephrased in a slightly different way than suggested, but we are confident that it is correct.

Referee 2:
Points 1 and 3 have been addressed including in the text the suggestions of the referee. Point 2: we have changed the phrase according to what requested by referee number 1 and are comfortable with the current version.

Referee 3:
Major comments: as already mentioned, we have already addressed these two points in the first revised version of the paper. Here follow a brief discussion of these two points.

1) We agree with this criticism. We have gone through the data again and conducted sensitivity analyses keeping patients with stage IV disease at diagnosis separate from the others. In fact, we have not found that these patients carry a more severe prognosis compared with patients with recurring disease after surgery of localized disease. Indeed, the “Stage at first diagnosis” variable does not affect response, time to progression and overall survival neither positively, nor negatively. We have therefore modified the discussion according to the referee’s comments.

2) The possible prognostic impact of prior exposure to taxanes in the adjuvant setting has been addressed in the discussion, as requested. As a variable potentially associated with clinical outcomes it must be noted that “prior taxanes” was analyzed both at Univariate and multivariate analysis and did not result significantly associated with overall survival or time-to progression. We agree that it could be interesting to compare the survival from the initial diagnosis of cancer (operable or initial stage IV) and we did it as requested. We did not find a difference, but, apart from curiosity, we do not feel that this finding should be included in a paper investigating treatment for metastatic disease. In fact, in operable patients, factors affecting the natural course of the disease before metastatic relapse should be included in the analysis. We thank the referee in any case because this is a very good suggestion for another paper focusing specifically on the issue of the natural course of HER2 positive breast cancer.

Minor essential revisions
1) The manuscript has undergone professional linguistic revision
2) We have renumbered figures into figure 1, 2 and 3 and changed the legend accordingly. We have changed “cum survival” into overall survival in the Y axis of figure 1b and 2.
3) The first sentence of the discussion has been rephrased in order to eliminate the verb “shows”.

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Write back
Discretionary revisions
   1) The reference to the pivotal trial has been added
   2) The manuscript has been corrected as suggested
   3) We have rephrased the whole sentence to improve readability. A.S. stands for Anna Sapino who is the pathologists carrying on FISH analyses. “A.S.” has been removed in order to avoid confusion.
   4) The referee is right, we meant Disease free interval. We have introduced the suggested change.