Title: HER-2, p53, p21 and hormonal receptors proteins expression as predictive factors of response and prognosis in locally advanced breast cancer treated with neoadjuvant docetaxel plus epirubicin combination

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Author's response to reviews: see over
Author's response to reviews

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Version: 1 date: 01/09/2007
Reviewer's report
Title: HER-2, p53, p21 and hormonal receptors proteins expression as predictive factors of response and prognosis in locally advancer breast cancer treated with neoadjuvant docetaxel plus epirubicin combination

Version: 1 Date: 29 October 2006

Reviewer: Susanne Taucher

Reviewer’s report:
General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Which procedure was performed to diagnose breast cancer.

   Open breast biopsy (incisional biopsy)

2. What was the rationale to give 9 cycles of chemotherapy?

   The rational to use 9 cycles of chemotherapy is based on Hortobagyi GE et al report (Cancer. 1988 Dec 15;62(12):2507-16) report. We are used to treat patients with high risk breast cancer with this approach since 1992.

3. Tumor diameter at the time of diagnoses should be described.

   We preferred not describe the tumor diameter at the time of the diagnosis. In fact, we omitted this data in the report because our inclusion criteria were based on clinical staging (TNM), and the tumor diameter is not the unique component in such staging procedure. However, the mean diameter was 6.03 cm (range 2.5 – 14.0 cm) and 33% of patients were N1 or N2.

   An axillary clinical down staging (N2 turns to N1 or N0; and N1 turns to N0) was necessary to classify as objective response, patients with positive axillary nodes (N1 or N2).

4. Did you evaluate menopausal status before and after chemotherapy?

   I evaluated the menopausal status only before chemotherapy and I included the data in the manuscript.

5. The authors stated that 60 patients were consecutively included in this trial. Which inclusion criteria were used?
Corrections were done (Patients and Methods).
Reviewer's report
Title: HER-2, p53, p21 and hormonal receptors proteins expression as predictive factors of response and prognosis in locally advanced breast cancer treated with neoadjuvant docetaxel plus epirubicin combination

Version: 1 Date: 21 November 2006

Reviewer: Sehwan Han

Reviewer's report:
General
The article analyzed not novel topic in breast cancer management albeit the conclusion was rather solid. Authors have to focus on the negative results of molecular predictive markers mentioned in the Discussion. Generally we can not get any unbiased solid conclusion from retrospective analysis. We can retrieve another hypothesis from the retrospective analysis of the data and this hypothesis generating role is a relevant one.
I recommend to revise the discussion and conclusion on the basis of negative results of predictive markers.

The discussion and conclusion were revised according to the negative results of predictive markers.

Additionally, I would like to recommend some points needed revision.

1. In the Discussion, the authors mentioned “HER2 expression is associated with resistance to anthracycline plus docetaxel.” The expression seems too conclusive because there are a lot of data to deal with the better clinical response to anthracycline of HER2-expressing tumors.

I could not find the expression “HER2 expression is associated with resistance to anthracycline plus docetaxel” in the manuscript. I found “The observation of HER-2 protein expression is a stable phenotype and the association between HER-2 overexpression and poor prognosis allows us to assume that patients with tumors overexpressing HER-2 are resistant to the taxane and anthraccline combination, as they did not benefit from this citotoxic treatment”. In fact, the HER-2 overexpression is the most important maker of chemotherapy resistance in our study. I revised the paragraph.

2. The authors emphasized the changes of p21 and p53 expression after neoadjuvant chemotherapy but not HER2. HER2 expression is a unique biologic features which is well maintained during breast cancer progression. Another biologic characteristics of HER2 is that majority of tumor have the same nature in HER2 expressing tumors. Thus, analysis about the change of HER2 expression is not needed nowadays.

HER-2 stable phenotype during neoadjuvant chemotherapy was reported by other authors. I revised the paragraph and I do believe that this stable phenotype is
due chemotherapy resistance. However, to confirm this finding, additional study must be carried out.

3. Please omit or reduce the talk about p21 and p53 which is not important.

   Done.