Author's response to reviews

Title: Higher rate of skin rash in a phase II trial with weekly nanoparticle albumin-bound paclitaxel and cisplatin combination in Chinese breast cancer patients

Authors:

Li Chen Tang (forever_drawer@163.com)
Bi Yun Wang (wangbivun@msn.com)
Si Sun (0356208@fudan.edu.cn)
Jian Zhang (drawer426@hotmail.com)
Zhen Jia (mark_xyw@hotmail.com)
Yun Hua Lu (mark_xyw@163.com)
Gen Hong Di (dgh_2011@yahoo.cn)
Zhi Ming Shao (zhimingshao@yahoo.com)
Xi Chun Hu (xchu2009@hotmail.com)

Version: 2 Date: 26 December 2012

Author's response to reviews: see over
Dear Editor,

It is our pleasure to receive the suggestions from you and the other reviewers. Thank you very much for your suggestions. As you mentioned, we have added the requested part, done some correction and answered the questions as expected. Here are the replies to the Editor and the Reviewers.

Editor

**We would like to ask for written consent to participate in the study was given by the patients.**

Answer: Written consent was attached as a figure file.

**We would like to ask for written consent for the publication of images was given by the patients.**

Answer: Written consent was attached as a figure file.

**Request for Trial Registration Number.**

Answer: Trial Registration Number was added in not only the abstract but also the Methods paragraph in the literature.

**Please provide improved rationale for conducting their study in the Background section.**

Answer: We have added a paragraph to further illustrate the study background in the Purpose part.

Reviewer: Vivek Roy

Major essential revisions:

The statement in introduction section - "Several large randomized trials documented improved efficacy and favorable safety...." is factually incorrect. There have been only limited randomized trials. One of the reference (#4) cited is not a randomized trial. This sentence and the reference need to be corrected.

Answer: We have changed the sentence and reference as ‘Several clinical trials [4, 5] documented the improved efficacy and favorable safety profile of nab-paclitaxel in the treatment of MBC.’.

Minor and essential revisions:

The relevance of the last paragraph in discussion section is unclear to me. I do not think this adds to the main point of the manuscript and should be deleted. There are several grammatical errors that I have indicated in the attached
document. I have also suggested some other changes in the document.

**Answer:** We have deleted this paragraph. We also have corrected the errors and make all the changes as instruction by the reviewer.

**Reviewer:** Valentina Nekljudova

- Major Compulsory Revisions

1. It is absolutely not clear from the abstract that the rate of skin rash in western patients treated with nab-paclitaxel is taken from the literature and not from the western patients treated in the same trial. It also should be mentioned as a limitation in the discussion section.

**Answer:** We have added a paragraph in the discussion section to illustrate the limitation of the skin rash rate cited from other literature.

2. The western patient skin rash rate itself is not given in the abstract, only a p-value is provided which depends not only on the effect size but also on the sample size and therefore standing alone tells nothing about the absolute difference.

**Answer:** We have added the western patients skin rash rate in the abstract and also a paragraph in the discussion section to explain the limitation of the citation.

3. It is not clear whether the analysis was performed after all patients completed (or discontinued) treatment or is it an unplanned analysis of a running trial.

**Answer:** The analysis was performed after all patients completed their treatment. Rash is an initially unplanned but later planned sub-analysis of the running trial, and we mention this point in the final paper.

4. In the discussion authors cite a review by Yamamoto[21] “including almost all studies related to nab-paclitaxel in breast cancer” saying that only approximately 4% patients developed skin rash globally, but the data in Table 2 on 229 western patients with nab-paclitaxel is taken from Table 5 of Yamamoto review which refers to only one particular study by Gradishar et al. (J Clin Oncol. 2005;23(31):7794–7803), with 3-weekly regimen of nab-paclitaxel. It should be mentioned explicitly. Authors should also explain the choice of this particular control group. Were no data on hypersensitivity reactions reported in other studies?

**Answer:** Although there are a few studies which focused on nab-paclitaxel regimen, there is limited literature reported skin rash presentation among them. Therefore, there must be limited choice in setting the control group. We have illustrated the limitation in the discussion part as expected.

5. Authors should discuss the potential bias caused by the differences between treatment regimens in Chinese and western patients (weekly vs
3-weekly, additional cisplatin) as well as in the definition of the considered endpoint (“skin rash” in this paper, “hypersensitivity” in Gradishar et. al).

**Answer:** We have added a part to illustrate the potential bias and the potential problem for the comparison.

6. Confidence intervals for rates should be included.

**Answer:** We have added the confidence intervals for rates in our paper.

- Minor Essential Revisions (not for publication)

1. Abstract, methods: “Patients who received a least” - > typo, “at least”.

**Answer:** The mistake has been corrected.

2. Mislabeled references in Table 2: Yamamoto [20] (must be 21 as in “References” section), Guan et al. [21] (must be 22), Seidman [22] (must be 23).

**Answer:** The mistake has been corrected.