Author's response to reviews

Title: Association of cytochrome P450 genetic polymorphisms with neoadjuvant chemotherapy efficacy in breast cancer patients

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Author's response to reviews: see over
2 May 2012

The Editors
BMC Medical Genetics

To the Editors:
Thank you for considering the revised version of our manuscript titled, “Association of cytochrome P450 genetic polymorphisms with neoadjuvant chemotherapy efficacy in breast cancer patients” for publication in BMC Medical Genetics.

We are thankful to the reviewers for reading and further providing their thoughtful comments on our previous draft. There are some changes required in this manuscript as requested by reviewers, and we have gladly considered theirs recommendations in preparing our revision. In the following pages, we have provided a point-by-point explanation of the changes made in response to the concerns. We hope that all these changes fulfill the requirements to make the manuscript acceptable for publication in BMC Medical Genetics.

Sincerely,
Alevtina Grishanova on behalf of the authors.
Head of Department of Xenobiochemistry
E-mail: agrish@soramn.ru
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Reviewer Luis Quiñones’s comments and authors’ replies

Discretionary revisions
I think the conclusion is not so strong because of the observed CI95% for the association with CYP2C9*2 polymorphism which is a quite wide range and very near to 1.0 in spite of the number of patients is bigger enough.
Response: We have included statistical parameters (OR and CI) in our conclusion for better interpretation. We hope it helps to elucidate our findings to the readers more clearly.

Minor essential revisions

Material and Methods
• The author should include the date and number of approval document of the local ethics committee.
Response: The information about the approval document of the local ethics committee has included in the manuscript: “The local ethical review boards approved the study protocol (Protocol N3 from 08.06.2005), and all patients provided written, informed consent before acceptance into the study in accordance with the Declaration of Helsinki.”

• The sentence “electrophoresis on 10% PAAG-TBE gels” should be changed by “PAGE on 10% TBE gels”.
Response: We agree with the reviewer’s recommendations, and have changed the sentence in manuscript.

Results and Discussion
• “CYP3A4*B” Must be changed by “CYP3A4*1B” (paragraphs 1 and 8).
Response: We thank the reviewer for his exactitude. “CYP3A4*B” was changed by “CYP3A4*1B” in paragraphs 1 and 8.

Conclusion
• Change the sentence “CYP2C9*2 polymorphism associated…” By “CYP2C9*2 polymorphism is associated…”.
Response: We agree with the reviewer’s recommendation and have changed this sentence in the manuscript.
Major compulsory revisions
The cited bibliography is too old, the newest reference is 2008 (only one). This issue is relevant in order to have a strong support of the discussion and the conclusion. Major revision of literature is required.
Response: We agree with the reviewer’s recommendations, and have updated references in the manuscript.

Reviewer Angela Roco’s comments and authors’ replies

Major Compulsory Revisions
1. To find a valid association from the clinical point of view is necessary to realize the statistical analysis with the group Complete remission (CR) and Partial remission (PR), and not include Stable Disease (SD) group in the analysis of polymorphism and response to chemotherapy.
Response: Neoadjuvant chemotherapy response was estimated according to WHO criteria by ultrasonography and mammography: Complete Remission (CR) when no breast tumour was observed; Partial Remission (PR) when the reduction in the tumour area was 50-100%; and Stable Disease (SD) when the tumour area was reduced 0-50%, Progressive Disease (PD) was recorded if the tumour area increased or if a new lesion was detected (this sentence has been included in the manuscript for better elucidation). So patients were divided into two groups (positive and negative) according to chemotherapy response. Patients with SD and PR both responded to the neoadjuvant chemotherapy but only with different efficacy. So patients with SD were included to “Positive Response Group”.

2. It is necessary to correct the analysis of the tables 3 and 4 with the information of the patients with chemotherapy with CR and PR and genotype. Genotypic analysis indicated in the tables 3 and 4 corresponds to the total of patients with cancer of breast (395 patients) and not only to 261 patients who received chemotherapy. ¿In Positive o Negative group included 134 patients who did not receive chemotherapy in Tables 3 and 4?
Response: We agree with the reviewer’s recommendation and have changed tables 3 and 4 in the manuscript. Table 2 describes genotyping analysis of 395 women with breast cancer, and tables 3 and 4 describe statistical analysis of association of chemotherapy efficacy and CYPs polymorphic variants in 261 patients with breast cancer who received neoadjuvant chemotherapy. Other 134 patients with breast cancer were excluded from analysis because they did not receive chemotherapy.

Discretionary Revisions
1. Some references are absent in the introduction
Response: We acknowledge the reviewer’s concerns and have added some references in the introduction.

2. To update references
Response: We agree with the reviewer’s recommendations, and have updated references in the manuscript.

Editorial Requirement:
Copyediting:
After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further.
We advise you to seek the assistance of a fluent English speaking colleague, or to have a professional editing service correct your language. Please ensure that particular attention is paid to the abstract.

Response: The manuscript was edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English speaking editors at American Journal Experts. We have editorial certificate from the American Journal Experts Certificate Verification Key: D39C-FE5A-5E17-219A-7F2F. Date Issued: December 6, 2011.

We hope that you and the reviewer will find the revisions sufficient and can now consider our manuscript fully acceptable for publication in the BMC Medical Genetics.

Sincerely,
Alevtina Grishanova