

Format for ANSWERING REVIEWERS

September 3, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: ACC of breast revise.doc).

Title: Adenoid cystic carcinoma of the breast: Recent advances

Author: Kosuke Miyai, Mary R. Schwartz, Mukul K. Divatia, Rose C. Anton, Yong Wook Park, Albert G. Ayala and Jae Y. Ro

Name of Journal: *World Journal of Clinical Cases*

ESPS Manuscript NO: 12344

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

(1) Table 1 is good, yet it is unclear the criteria of trials included in this table. It would be good to have a systematic review approach in including the trails for a comprehensive picture of the disease.

Reply: We decided to include only recent (from 2010) data in Table 1, because 1) clinicopathological data based on large patient cohorts have been described only in the recent studies, and 2) Treatment could be different between the present and the past. According to the comments, we have added the criteria of trials included in Table 1 (“Epidemiology”, page 4, lines 6 and 7).

(2) It would be interesting to discuss more on the functional role of the ER- α 36 variant in ACC which shine light on the therapeutics in treating this disease. Available trials and any relevant biologics are needed to expand in this area in this review.

Reply: According to the comments, we have added the sentence regarding more detailed functional roles of ER- α 36 from the viewpoint of a possible antiestrogen based therapy for

breast adenoid cystic carcinoma (“Molecular genetic features”, page 11, lines 10 to 17).

(3) Breast cancer is well known to have some genetic factor, e.g. BRCA1, how is the hereditary background for ACC?

Reply: According to the comments, we have added the paragraph regarding the hereditary background of ACC of the breast (“Molecular genetic features”, page 10, line 25, and page 11, lines 1 to 5).

(4) Next-generation sequencing (NGS) has depicted a number of cancers and diseases, how is the progress of NGS on this rare cancer?

Reply: To our knowledge, there has been no study using NGS for ACC of the breast. According to the comments, we have added the sentence regarding this fact and added references 47-49 (“Molecular genetic features”, page 9, lines 5 to 11).

(5) What are the limitations of this review?

Reply: According to the comments, we have added the sentence regarding the limitations of this review (“Conclusion”, page 15, lines 8 to 10).

(6) The title is "Recent advances", yet still some more studies and references can be referred, some examples list below but not exclusive:

- Ross JS, Wang K, Rand JV, et al. Comprehensive genomic profiling of relapsed and metastatic adenoid cystic carcinomas by next-generation sequencing reveals potential new routes to targeted therapies. *Am J Surg Pathol.* 2014;38:235-8.
- Stephens PJ, Davies HR, Mitani Y, Van Loo P, Shlien A, Tarpey PS, Papaemmanuil E, Cheverton A, Bignell GR, Butler AP, et al. Whole exome sequencing of adenoid cystic carcinoma. *J Clin Invest.* 2013;123:2965-8.
- Cho WC. MicroRNAs: potential biomarkers for cancer diagnosis, prognosis and targets for therapy. *Int J Biochem Cell Biol.* 2010;42:1273-81.
- Daa T, Nakamura I, Yada N, et al. PLAG1 and CYLD do not play a role in the tumorigenesis of adenoid cystic carcinoma. *Mol Med Rep.* 2013;7:1086-90.

Reply: According to the comments, we have added these articles and other new articles as references (No. 20, 21, 31, 32, 47, 50-52, 62-65, 90-92) and discussed about them in the manuscript. We have not included the study by Daa et al (Mol Med Rep. 2013) in this review, because the study showed a negative result and investigated ACC of the salivary gland (not breast ACC).

3. References and typesetting were corrected.

We hope the corrections that we have made are satisfactory to you. If there are insufficient points in the corrections, please let us know. We are looking forward to hearing your favorable decision.

Thank you again for publishing our manuscript in the *World Journal of Clinical Cases*.

Sincerely,

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