

Format for ANSWERING REVIEWERS

March 10, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 9093-revised version.doc).

Title: Mechanisms and Therapeutic Advances in the Management of Endocrine-Resistant Breast Cancer

Author: Meng Zhao, MD, PhD; Bhuvaneswari Ramaswamy, MD, MRCP

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 9093

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) Reviewed by 00742507

“It is an excellent, fully up-to-date review of one of the most important subjects in breast cancer treatment. All aspects are covered, including positive and negative results. Good mixture of relevant literature. Conclusion: Accept”

Author’s response: We appreciate the reviewer’s comments and interest in our manuscript. We thank the reviewer’s support for our manuscript to be published in World Journal of Clinical Oncology.

(2) Reviewed by 00532382

“Very interesting, well thought out and organized. To publish. Conclusion: Accept”

Author’s response: We thank the reviewer for finding our review topic interesting and supporting our manuscript to be published in World Journal of Clinical Oncology.

(3) Reviewed by 02467561

“GENERAL COMMENTS: Dear Authors, the manuscript “Mechanisms and Therapeutic Advances in the Management of Endocrine-Resistant Breast Cancer “ is very interesting and exhaustive in its contents, focusing on novel strategies to overcome therapeutic resistance. Nevertheless, on my opinion, it is characterized by several critical points, which should be addressed before taking it into consideration for publication. SPECIFIC COMMENTS: TITLE The title reflects the major topics and contents of the study. ABSTRACT The abstract gives a clear delineation of the research background and objectives, but methods and conclusions should be more detailed”.

Author’s response: We appreciate the reviewer’s comments. We expanded the methods and conclusions in the Abstract as the reviewer suggested.

“MANUSCRIPT The manuscript is not well organized and structured. In particular: At the end of

the Introduction section, the appropriate references of the paragraph “A plethora of mechanisms have been proposed to explain resistance to endocrine therapy, including deregulation of various components of the ER pathway itself, activation of escape pathways that provide tumors with alternative cell proliferative and survival stimuli, alterations in cell cycle and apoptotic machinery, modulation in epigenetics and microRNA profile” should be inserted.”

Author’s response: we added the appropriate references of this paragraph.

“The Methods section is missing. It should describe in detail how the study was developed and carried out: the electronic databases used for the literature search (ie Medline, Cochrane Library, Scopus...); the time interval considered; the search string used; the criteria to identify and select the studies to be included in the review; how the assessment of the eligibility of the studies and the data extraction were performed.”

Author’s response: We added the Methods section. We included the databases, time interval considered, search string and review criteria used when we reviewed the literatures systematically.

“The results are not organized in a specific Results section and do not report the findings of the literature search and the selection process (i.e. the number of potentially relevant articles yielded by the search strategy; the number of the paper excluded on the basis of the inclusion criteria; the final number of the papers included in the review)”.

Author’s response: In this Review article, we report the findings of the literature search and analysis in detail. We summarized of the complex genomic and epigenetic regulatory pathways involved in endocrine resistance. We provided overview of the emerging targeted agents, including the completed and ongoing preclinical and clinical studies involving these novel targeted agents that we hope will improve the clinical outcome of patients with endocrine resistant breast cancer. We believe that the request made by the reviewer is more appropriate for a meta-analysis and contend that we have provided a very comprehensive review of the topic of endocrine resistance.

“Furthermore, the results of the reviewed clinical trials should be reported in a more organized and concise way.”

Author’s response: We have revised the table summarization of the results of the reviewed clinical trials. We classified these agents into three conceptual categories: agents targeting receptor tyrosine kinases signaling pathways including the PI3K/AKT/mTOR, IGF, FGF signaling pathway; agents targeting cell cycle regulators; agents targeting epigenetic regulation (table 1). Highlights on the clinical efficacy results of completed clinical trials testing these agents are included. The preliminary result, status and trail registry number are provided for ongoing trials.

“The Discussion section is missing. It should describe and discuss the added value of the study and the full public health implications of the study findings.”

Author’s response: We have included discussion of our review conclusion and future direction in the Conclusion section. Once again as this is a review article we contend that a separate discussion session is not necessary.

3 References and typesetting were corrected

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

Sincerely yours,



B. Ramaswamy.