Author's response to reviews

Title: PARP inhibitors in the management of breast cancer: current data and future prospects

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Author's response to reviews: see over
8th July 2015

Claire Barnard, PhD
BMC Medicine Editorial Office
236 Gray's Inn Road
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Dear Claire,

We appreciated the very thoughtful reviews of our invited manuscript, “PARP inhibitors in the management of breast cancer: current data and future prospects”.

We felt that the suggested revisions could add to the quality of our review, and we addressed them in this revised version of the manuscript.

Regarding comments by Reviewer 2:
Comment 1:
A figure has been created to support the paragraphs regarding PARPs’ intervention in DNA damage repair and the synthetic lethality concept in BRCA mutated cancers.

Comment 2:
In the paragraph discussing candidate biomarkers for predicting response to PARP inhibition, data from PrECOG 0105 and GeparSixto studies presented at ASCO Annual Meeting 2015 have been added. Data recently published on study TBCRC009 (Isakoff et al. JCO 2015) have been added as well.

Regarding comments by Reviewer 3:
Comment 1:
A figure has been created to support the paragraphs regarding PARPs’ intervention in DNA damage repair and the synthetic lethality concept in BRCA mutated cancers.

Comment 2:
Data from Coleman et al. (Gynecologic Oncology 2015) have been added to the discussion about single agent veliparib.

Comment 3:
Reference to data presented by Pahuja et al. at ASCO Annual Meeting 2015 have been added to the section of PARP inhibitors in combination therapy. Data from Rodler et al. JCO 2014 were already reported in table 3, but a reference in the text has also been added;

Comment 4:
Consistent use of abbreviation to describe germline BRCA mutation in table 1 has been verified. The chapter on potential resistance mechanisms has been expanded; Table 6
already contained all the potential resistance mechanism cited in the manuscript and has been left unaltered.

Comment 5:
The chapter on potential resistance mechanisms has been expanded and modified to be more clear.

Comment 6:
Line 17 on page 13 has been eliminated after revision of the paragraph according to Reviewers’ comments.

Regarding comments by Reviewer 4:

Comment 1:
The paragraph about PARP inhibitors’ mechanisms of action (catalytic inhibition and PARP trapping) have been expanded. In the chapter on PARP inhibitors in combination therapy, a discussion about the impact of PARP inhibitors mechanisms of action on synergy with chemotherapeutic drugs and safety has been added.

Comment 2:
The chapter on potential resistance mechanisms has been expanded. Table 6 already contained all the potential resistance mechanism cited in the manuscript and has been left unaltered.

Comment 3:
In the paragraph discussing candidate biomarkers for predicting response to PARP inhibition, data from PrECOG 0105 and GeparSixto studies presented at ASCO Annual Meeting 2015 have been added. Data recently published on study TBCRC009 (Isakoff et al. JCO 2015) have been added as well.

Comment 4:
The manuscript has been thoroughly reviewed for consistent grammar and punctuation.

Furthermore, the list of active phase II-III trials (both in the text and in tables 1 and 4) has been modified to reflect updated since submission of the first version of the manuscript; in the chapter on the possibility to expand use PARP inhibitors beyond BRCA-associated breast cancers, a discussion on HRD score has been added, together with new insights from AACR and ASCO 2015 annual meetings.

Minor styling edits have been done to better harmonize the changes made in response to the reviewers’ comments.

We have made sure that the manuscript conforms to the journal style.

We hope that you and the reviewers are satisfied with the revisions, and we look forward to hearing from you with your thoughts.

Best regards,

Judy E. Garber, MD MPH

Luca Livraghi, MD