

Peer Review File

Article information: <https://dx.doi.org/10.21037/cco-23-22>

Reviewer A

I have only minor point for authors considerations that could potentially increase the strength of this manuscript, but I understand this is a critical evaluation of the current available evidence.

1. would authors consider on figure one to show somehow which chemotherapy agents they would recommend in combination once in a few of them the benefit for HR+ tumour as mono therapy is marginal?

Thank you for this comment. Unfortunately, these agents in combination are marginal as well, and rather than adding efficacy only add toxicity. We have added this element to our manuscript.

2. could the authors consider for this, or a subsequent paper, to include a section discussing their recommendations for different realities once many countries will not be able to replicate this perfectly suggested treatment sequence?

Again, a wonderful comment. We would love write a follow up global perspective on this sequencing piece (adding a few global voices to our authorship), but to include some any different states—from variable approvals across US and EU, access in LMIC, and other issues including access, cultural preferences, and epidemiological differences, we can not include that here and come near word limit.

3. could I suggest for the authors to consider a section to approach when is time to cease systemic treatment for metastatic breast cancer, especially now that we have quite a substantial range of options available?

We have added this section as recommended, but it extended the word count well beyond what CCO originally proposed. We will defer to editorial team if they feel this added language warrants the additional word count.

4. Could the authors consider for this or another publication a discussion on how the patients that experienced early progression on CDK 4/6 should be approached? Perhaps to consider building in the already comprehensive nice figure 1?

Added a sentence to the section included for answer #3 above.

5. Finally, I apologise if this is in the manuscript and I missed but to my eyes very little seem to be discussed in terms of long term responders and oligo progression. Although not the vast majority, they are not infrequent and perhaps the authors could consider adding sections if they feel appropriate.

Yes. Indeed, very little phase 3, randomized data exists, so the topic ends up being some expert opinion and may not mix well with a true review. Authors added a few lines into the additional section discussed in answer #3 above.

After this very minor points to be considered by the authors I would be happy to review this article. Thank you for your time and effort with the review, and for your confidence in our manuscript—it would certainly be an honor to extend our writing with many of the elements you mention. As I am

sure you know, so often we are limited by word counts. Each of your comments could make wonderful topics to explore fully.

To the editors—perhaps this insightful reviewer should be invited to author in their own right!

Reviewer B

1. HR/MBC should be defined upon first use in the Abstract. **Updated.**
2. PI3K/AKT/PTEN should be defined upon first use in the Main Text. **Updated. Please note AKT has no definition—it is simply “AKT”.**
3. All the abbreviations in the figure and table should be defined in the explanatory legend. **Updated.**