Reviewer’s report

Title: Safety, activity and molecular heterogeneity following neoadjuvant non-pegylated liposomal doxorubicin, paclitaxel, trastuzumab and pertuzumab in HER2-positive breast cancer (Opti-HER HEART): an open-label, single-group, multicenter, phase 2 trial

Version: 0 Date: 03 Oct 2018

Reviewer: Judith Bliss

Reviewer's report:

A nice manuscript and a few suggestions for improvement.

1) "objective" and "endpoints" & "outcomes" used interchangeably and conversely - the objective of a trial can be achieved by testing a null hypothesis on data collected for specified endpoints - rationalise language accordingly including that a trial can "meet" an objective not "meet an endpoint".

2) Abstract defines Type A and Type B cardiac events - these are not referred to in the main text

3) pCR / ORR etc are activity related endpoints not efficacy (this is not a comparative trial with PFS type endpoint)

4) Further justification for the statistical design would be reasonable - the absolute rate of cardiac events will be heavily influenced by age and other demographic factors and thus where there is no control group consideration should be given as to whether the "control" rates observed in other trial is applicable to this patient population - who were generally quite young. Furthermore given the relatively small sample size the number of observed events results in a lack of precision of the estimated rate. this should be acknowledged.

5) Results - please include n cases when reporting results not just the %.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Not applicable

Are the conclusions drawn adequately supported by the data shown?
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Yes

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