Reviewer’s report

Title: Breast Cancer in Ethiopia: Evidence for geographic difference in the distribution of molecular subtypes in Africa

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Reviewer: Saraswati Sukumar

Reviewer's report:

The authors report on a study conducted on the incidence and molecular types of breast cancer in Sub-Saharan Africa, and to compare the results to published work mainly from Western and Central Africa that show that breast cancer occurs at younger ages, presents with aggressive features that include high-grade, advanced stage and triple-negative phenotype (negative for ER, PR and HER2). Data, though limited, does exist from East Africa including Ethiopia that shows that hormone receptor negative tumors account for a lower proportion of all breast cancers compared to the rest of Africa. For example, of 352 cases (BMC Cancer. 2014 Nov 29;14:895), Yonas et al published that 65% were ER+. Similarly, nearly 70% were found to be ER+ in an other study (Newman, LA); similar results were reported on 186 women of Ethiopian origin living in the US (78% ER+, 22% ER-); Breast Cancer Res Treat. 2012 Oct;135(3):867-73). No HER2 evaluation was reported. In this paper, breast cancer patients (n=114; years 2012-2015) were examined for ER, PR, Ki67 and HER2 receptor status using immunohistochemistry from tissue microarrays. In equivocal tumor samples, FISH was used for assessment of gene amplification and for confirmation in HER2-enriched cases. They expressed the results using the St. Gallen model and found: Luminal A and B formed 66% of the cases, HER2 enriched 10%, and TNBC 23%. The manuscript is written well and data presented logically and confirms previous findings while reporting on the HER2 status as well.

A major concern with this paper is the use of tissue microarrays to perform the studies. ASCO guidelines state that sections of multiple core biopsies should be used to accurately assess percent positive for the various markers. In most other studies, whole sections of the surgical blocks are used to circumvent problems in cell numbers. Were whole sections used first to determine the concordance in calls in a pilot before embarking on this study. How many epithelial cells were counted in order to deem them positive or negative? How did FISH results look on the small 6 mm spots? Since none of this data is presented it is not possible to assess accuracy.

The second concern is that that the study is small n=114, and the results are at best, again interesting, but not reliable. The HER2 results are new, but the methods used make it difficult to interpret.
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.

No

Are the conclusions drawn adequately supported by the data shown?
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No

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