Reviewer's report

Title: Mortality risk of black women and white women with invasive breast cancer by hormone receptors, HER2, and p53 status

Version: 1 Date: 1 January 2013

Reviewer: Vincent Caggiano

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General Comments:
This study addresses an important topic in breast cancer mortality, that is, to what extent do ER/PR/HER2 subtypes and p53 protein overexpression affect the black-white disparity in mortality, specifically in the triple negative and Luminal A subtypes. Unfortunately, the study fails to show convincing, statistically valid evidence that any black-white disparity exists other than in all-cause mortality.

Participants in this study were breast cancer patients enrolled in the Women's Contraceptive and Reproductive Experiences (CARE) study from July 1994 through April 1998 randomly sampled from five field sites: Atlanta, Detroit, Los Angeles, Philadelphia, and Seattle. Black women were oversampled to maximize their numbers. Although this may be a valid statistical maneuver, it speaks to the lack of black participants in clinical trials and casts doubt on the applicability of results being attributed to the overall US. population.

On the positive side, the paraffin-embedded tumor blocks from Detroit and Los Angeles at the University of Southern California centralized laboratory, a major plus for this study.

Major Revisions
1) In the Abstract, under Results, the authors state "this black-white difference among older women was confined to those with Luminal A/p53- tumors (breast cancer-specific HR 1.89; 95% CI, 0.93 to 3.86; all-cause HR 2.22; 95% CI, 1.30 to 3.79)". While the all-cause HR is statistically significant, the breast cancer-specific HR is not, and should so state.

2) Under Results, Black-white differences in breast cancer-specific mortality, 2nd paragraph, it is stated "the observed black-white differences in breast cancer-specific mortality were attenuated after additionally controlling for tumor stage". This is a gentle way of saying that statistical significance disappeared. It does not address the fact that blacks are more likely than whites to present with advanced stage of disease (Ref. Li CI et al. Arch Intern Med 2003; 163: 49-56), hence the loss of statistical significance when controlling for stage.

3) Under Discussion, 4th paragraph (limitatuions). there is no discussion why all-cause mortality is different from breast cancer-specific mortality. No mention of comorbidities (Ref: Tammemagi CM et al. JAMA 2005; 294: 1765-1771). Also
there is no discussion why p53- (lack of overexpression) should have a negative effect on mortality or survival when p53 mutations (as correlated with p53 overexpression in tumor tissue) are associated with resistance to chemotherapy, radiation therapy, and poor prognosis, as stated in Background, 4th paragraph.

Minor revisions

1) Background, 3rd paragraph. It is stated that TN breast tumors account for 10-30% of all invasive breast cancer (6, 15):. Most studies show that TN breast cancer is in the range between 10-25% of the population depending upon the demographics of the population (Ref Bauer KR Cancer 2007; 109:1721-1728; Perou CM The Oncologist 2011;16(suppl 1):61-70). The 30% is from the LA County component of the Women's CARE Study referred to reference 6 of the manuscript. these were women for whom mammograms were obtained, and once again this may not truly reflect the overall population.

2) Methods, 1st paragraph. Why were LA and Detroit selected for study, and why were Philadelphia, Atlanta, and Seattle excluded. Was this due to funding constraints? Would results have been different if all sites were included, or if Atlanta, or Philadelphia, or Seattle were chosen instead of Detroit? Or instead of LA? We are left to decide if this subset analysis is valid.

3) Methods, 1st paragraph, when discussing race. According to reference 37, Table 2, #4: white or black race (including Hispanic ethnicity). No mention at all as to if and how this categorization may affect results.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.