Reviewer's report

Title: Association of MTHFR Gene Polymorphisms with Breast Cancer Survival

Version: 1 Date: 21 July 2006

Reviewer: Martha Shrubsole

Reviewer's report:

This report describes the association of MTHFR genotypes/diplotypes with overall breast cancer survival. The study population consists of surgical breast cancer cases from Baltimore, Maryland, USA. Strengths of this study include a large proportion of African American cases. The study is limited by its small sample size, particularly in subgroup analyses.

Minor Essential Revisions

1. Presumably few eligible women died prior to recruitment if recruitment occurred within 6 months of diagnosis. For those cases that were deceased but otherwise eligible, were they included in the study or current analysis? If not, how many were excluded?

2. The mean follow-up time is given. With the long recruitment period (10 years) it would be helpful to include some more information about the distribution of follow-up time. Please also give the median follow-up time.

Major Compulsory Revisions

1. The number of deaths (59) is given in Table 1, but the number of breast cancer deaths, the analysis events according to the methods section, is not. It would be helpful to have the person-years and number of events added to Tables 3-5. Having the sample size available would allow the reader to evaluate the context of the findings. Also, is information on disease-free survival available in this population?

2. It is possible that the relationships with ER(-) cancers are due to differences in chemotherapy treatment or stage, both of which are strongly related to survival. The authors stated they evaluated interactions of ER status with chemotherapy. Although the sample size is small to evaluate any interaction, did the authors evaluate an interaction of MTHFR with TNM stage? Likewise, the authors state that few in their study population used MTX/5-FU, so it seems that they have specific information on chemotherapy modalities. If these data are available, the information should be added to Table 1. Was the null interaction between ER status and specific chemotherapy regimens or was it only evaluated for any chemotherapy?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.