Reviewer's report

**Title:** Genetic polymorphisms in the endothelial nitric oxide synthase gene correlate with overall survival in advanced non-small-cell lung cancer patients treated with platinum-based doublet chemotherapy.

**Version:** 1  **Date:** 4 June 2010

**Reviewer:** Sharon Pine

**Reviewer's report:**

This report shows an association between the VNTR polymorphism in intron 4 of the gene encoding eNOS and lung cancer survival. While the results are interesting, the study is small and as the authors pointed out, the interpretation should be taken lightly until the polymorphism is examined in an independent and larger cohort.

Showing an association between a functional variant that gives rise to an RNA species that inhibits eNOS, and lung cancer survival is very exciting and opens the door to new research areas studying the effect of small RNAs in cancer patients.

**Minor essential revisions**

1. PS and HR in abstract needs to be defined
2. Stratify patients into adenocarcinoma (80% of patients) and known non-adenocarcinoma. While there would not be enough power to show a significant interaction, the results could show a trend of whether the observed results were driven by the adenocarcinomas.
3. Likewise, because of the association between NOS and inflammation, stratify patients by smoking status. The results might provide clues into how the repeat variant affects eNOS in a heightened inflammatory state.
4. Demonstrate why additional co-variates were not included in the model – age, gender, histotype, stage. Even if there is insufficient power to observe an effect of these variables on survival, they may be confounding. The authors state that additional clinical factors were included in the model but they were not clearly defined.
5. Show the HR for females and stage III disease, since the associations were significant among males and stage IV disease.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests