Reviewer's report

Title: Genotypes and haplotypes of the VEGF gene and survival in locally advanced non-small cell lung cancer patients treated with chemoradiotherapy

Version: 1 Date: 23 June 2010

Reviewer: Katsuhiro Masago

Reviewer's report:

Comments to the authors:
This study of patients with locally advanced non-small cell lung cancer who received chemoradiotherapy evaluated VEGF polymorphisms for their prognostic impacts. In this study, Guan et al. demonstrated that among three regulatory VEGF SNPs (-460T>C; -634G>C; 936C>T), the -460 CT and CC genotypes were significant independent prognostic factors for survival.

Major Compulsory Revisions:
1. The reason why the authors selected only these three SNPs is unclear. I think more precise explanations for the selection of these SNPs are necessary in the Introduction. For example, the authors should describe how these regulatory SNPs affect the production of VEGF in vitro and the frequency of the minor allele of each SNP in the Asian population.

2. In recent years, the method of real-time PCR with the 5'-nuclease assay (TaqMan) seems most frequently used for SNP genotyping due to the technique’s accuracy and reproducibility. In this study, RFLP was selected for genotyping. Thus, more precise details about RFLP methods are required, including primer design, kinds of restriction endonucleases used, and PCR conditions. Electrophoretic figures are also needed.

3. It seems unreasonable to put patients with stage IIIa and IIIb in the same cohort, although the authors use staging as a factor in multivariate analysis, which appears to maintain the independence. Rather, I believe the reader will want to know the influence that the SNP has on survival of stage IIIa. It seems that the survival impacts will become clear when the authors separate stages IIIa and IIIb into two cohorts.

4. More fundamental discussion about how the -460C allele affects the prognosis is necessary.

5. Each Kaplan Meier curve requires stating the number of censored patients and the 95% confidence interval of median OS so that readers can inspect the reliability of the analysis results.

Minor Essential Revisions:
1. In the abstract, page2, line 2, a definition of the abbreviation "VEGF" is necessary.
2. In the abstract, page 2, line 12, definitions of the abbreviations "HR" and "CI" is necessary.

3. In the abstract, page 2, line 5, it seems that name -460T>C is generic rather than -1498T>C.

4. The authors should mention if a new classification for Staging was used.

**Level of interest:** An article of limited interest

**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.