Reviewer's report

Title: Prognostic significance of composite expressions of MCM2, Ki-67 and gelsolin in non-small cell lung cancer

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Reviewer: Cheng-long L Huang

General

Authors performed a clinical study on expressions of MCM2, Ki-67, and gelsolin in NSCLC patients, and concluded that composite application of these biomarkers of greater value than single marker application in assessing a prognosis of NSCLC patients. Each biomarker might have some clinical impact on NSCLC patients. However, only gelsolin proved to be a significant prognostic factor for a poor prognosis in NSCLC patients in this article. In addition, there are many statistical problems to be corrected in the present form.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The MCM2 expression and the Ki-67 expression are associated with the tumor proliferation rate. How about the relationship between these biomarkers and tumor status? The results about tumor status can be demonstrated in Table 1 and Table 2.

2. The gelsolin expression is associated with tumor motility and metastasis. How about the relationship between the gelsolin expression and nodal status? The results about nodal status can be demonstrated in Table 1 and Table 2.

3. In general, the prognostic significance should be analyzed by a survival curve, Log-rank test, and Cox hazard model. The analyses of vital status (page 11 line 15 to 16 and Table 1) are meaningless and should be deleted.

4. In page 11 line 16 - 18, the statements about survival are somewhat confusing. Only gelsolin expression had a significant difference in mean survival time. In contrast, there was no significant difference in survival time according to the MCM2 expression or the Ki-67 expression.

5. In page 11 line 18 - 20, the statement about the correlations between MCM2 and gelsolin, Ki-67 and gelsolin should be deleted because R=0.14 and R=0.13 are too low to demonstrate the correlation between them.

6. Regarding composite analysis about survival (from page 12 line 11 to page 13 line 5, and Table 3, Figure 2), these statements are rather confusing. Only gelsolin proved to be a significant prognostic factor for a poor prognosis in NSCLC patients in this article. For example, patients with GSN high and Ki-67 low had a worse prognosis than patients with GSN high and Ki-67 high. Patients with GSN high, Ki-67 low, and MCM2 low and patients with GSN high, Ki-67 low, and MCM2 high had a worse prognosis than patients with GSN high, Ki-67 high, and MCM2 high. Authors should re-analyze these data and clearly summarize results again. I guess that the multivariate analysis using some composite scoring of these biomarkers might be useful. In addition, survival curves of other groups of patients, not only in both low and both high, should be demonstrated in Figure 2.

7. In page 14 line 20, there were several clinical studies demonstrating the clinical significance of the Ki-67 index in NSCLC patients, not only in gastric cancer. Authors should cite these previous clinical studies in NSCLCs.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The description of methods is too long and could be shortened. For example, 男性 and 女性, Caucasian and non-Caucasian, smoking status, duration of smoking, average packs of cigarettes smoked, which are clearly described in Table 1, could be deleted from page 7.

2. In page 9 line 1, the finding of immunohistochemistry had better be evaluated independently by two investigators.

3. The description of results about patient characteristics (from page 10 line 7 to page 11 line 2) is too long and clearly described in Table 1, and they should be shortened.

4. In page 11 line 4 - 6, there are missing labels on Figure 1.

5. In page 11 line 6, which is correct, 47% or 61.7% (in Table 1)?

6. In page 12 line 15, 低 Ki-67高 is 高 Ki-67低, isn't it?
Discretionary Revisions (which the author can choose to ignore)
The analyses of survival according to pathological stage, such as early stage I or advanced stage II to III, might be useful (Huang et al, Br J Cancer 92:1231-1239, 2005).

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: Yes

Declaration of competing interests:
I declare that I have no competing interests.