Reviewer's report

Title: Prognostic value of secreted phosphoprotein-1 in pleural effusion associated with non-small cell lung cancer

Version: 1 Date: 2 October 2013

Reviewer: Georgios Stathopoulos

Reviewer's report:

RE: MS #1786281182106762

Zhang et al., Prognostic value of secreted phosphoprotein-1 in pleural effusion associated with non-small cell lung cancer

COMMENTS TO AUTHORS

With great interest I reviewed the above-referenced manuscript, which reports on the levels of osteopontin in malignant pleural effusions (MPE) as a means to assess prognosis. The authors tested a reasonable sample size and used appropriate controls and methodology, to determine the prognostic significance of osteopontin in this patient population. This is a timely and valuable addition to the literature, since osteopontin is intimately linked with MPE biology and prognostic markers in patients with MPE are lacking. In specific, osteopontin was recently shown to be highly important in adenocarcinoma-induced MPE formation (Psallidas I et al. Secreted phosphoprotein-1 directly provokes vascular leakage to foster malignant pleural effusion. Oncogene 2013;32:528-35). However, the molecule does not appear to possess diagnostic significance for MPE, since many pleural effusions share high osteopontin levels (Moschos C et al. Osteopontin is upregulated in malignant and inflammatory pleural effusions. Respirology 2009;14:716-22). There is only one study addressing the prognostic value of serum osteopontin in patients with lung cancer undergoing surgery (Takenaka M et al. Serum level of osteopontin as a prognostic factor in patients who underwent surgical resection for non-small-cell lung cancer. Clin Lung Cancer 2013;14:288-94). The authors showed osteopontin to be a marker of poor prognosis, and that is was specifically associated with pleural invasion. Hence the idea that osteopontin, as measured in the pleural fluid, could reflect the tumor burden, and could be a prognostic marker in MPE is a brilliant idea. The methods employed by the authors to test this hypothesis are sound and their results are reasonable and well-interpreted. Minor comments for revision, outlined in the comments to authors, could enhance the overall impact of the manuscript.

MINOR COMMENTS

1. Was this a retrospective study on a biobank or a prospective one? This should be stated in the methods and the abstract.

2. Did the authors measure serum osteopontin levels? They may also be of prognostic value as in the above study. If the authors have serum samples, it may be a valuable addition to the dataset. If not, the authors might state in the
discussion that this may be a valid research question for future studies.

3. Were pleural fluids collected during diagnostic or follow-up thoracenteses?

4. Were SPP1 data normally distributed? If not, the authors should use Mann-Whitney instead of t-test.

5. Are the data shown as mean±SD or SEM? This should be stated in the methods (stats).

6. The methods section should be subdivided into subheadings such as: study patients or protocol, measurements, statistics, etc.

7. The SPP1 values of control and study patients should be given in a new figure in the form of a dotplot, so the reader can appreciate the overlap of data between the two groups.

8. Symbols should be explained in tables, and axes should be more clearly labeled in graphs (ie, spell out acronyms and indicate the units, ie progression-free survival in days).

9. What is progression-free survival for a patient with MPE? Please define in methods.

**Level of interest:** An article of outstanding merit and interest 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.