Reviewer's report

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

Version: 1 Date: 8 October 2013

Reviewer: Jordan Olson

Reviewer's report:

This paper has very good data in it, and the basic premise and study design is sound. However, the paper is confusing and needs some major revisions prior to being published. I would strongly encourage the author to make the necessary revisions and resubmit. Perhaps narrowing the scope of the paper to just look at the diagnostic value of SPP1 in pleural effusions would be helpful, as there seems to be some controversy in this area.

Major Compulsory Revisions

The background section could be significantly shortened as it currently discusses malignant pleural effusions at length without a clear direction. The discussion of SPP1 protein is good, but also could be shortened. It is not clear how these 6 paragraphs add to the main point of the paper – 2 or three paragraphs may be sufficient.

Please describe the features of both the study patients and the case controls in a table. This is done for the study patient’s but the case controls are neglected, and no comparison is made between case-controls and study patients. These features should not be in the methods section.

You mention larger sample sizes needed in your discussion – was a power calculation performed to define your enrollment numbers? If not, could you perform one and show that the study was appropriately powered?

Please define the pathologies of the case-control group.

Please describe how pleural effusions are collected (bottle, additive solution, etc).

A pilot experiment is mentioned in the methods section. Can more details be given about this, or a summary of the results? It seemed to influence the way the assay was run, (dilution) differently from how the assay directions state, although you mentioned that the manufacturers instructions were followed.

The positive/negative disease state is not stated for the ROC curve analysis. (it can be inferred, but it would be better if it was stated).

It might be helpful to had a box plot/dot plot of concentrations of SSP1 vs. malignancy so the actual concentrations can be compared, in addition the the
means and standard deviations.

The results and discussion says that SPP1 is correlated with prognosis and extra pulmonary metastases – could you include these correlation graphs and coefficients?

The paragraph about pleural fluid analysis on page is confusing and contains many grammar mistakes. I think you mean that to diagnosis a malignant pleural effusion you need to perform thoracentesis or pleural biopsy, but it currently reads that a physician need to do these things to diagnosis any effusion.

Could you describe why your results on SPP1 concentration in malignant vs. non-malignant differ from 1 of the other studies which did the same sort of study you performed? Also discuss the study with results that agree with your results?

The discussion talks about the case control patients, but does not give a pathogenesis of why SPP1 is elevated in these patients.

Your conclusion says that it ‘may provide an auxiliary diagnostic modality” and an increased level ‘may be an indicator of poor prognosis, when your in your results section you say that the differences in survival were statistically significant. These statements are contradictory, and deal with the main theme of your paper.

Minor Essential Revisions

Many formatting/typos in abstract – mainly missing spaces.

No need to use ‘however’ on page 4 in the last paragraph of the discussion.

In the first paragraph of the methods section it mentions pleural biopsy, but then discusses that all pleural fluid had positive cytology. This is confusing.

Overall the language is acceptable, but not fluent. Perhaps a native English speaker with knowledge of the topic could be recruited to assist with the flow.

Typos in 2nd paragraph page 10

The review of pathogenesis of Malignant pleural effusion is very good, however, I’m not sure how it directly relates to results of this study, or is derived from the results of this study. While good, it may not be needed.

Please write out what you mean by PFS and CUM Survival and survival functions on your survival curves.

Discretionary revisions:

Keywords of ‘prognosis’ and ‘auxiliary diagnosis’ may be over-broad.

Was the serum levels of SPP1 measured for this study (or could biorepository/historic samples be used to assess it in the study patients?) It would be very good to compare serum vs. pleural concentrations.
Page 10 - word “effusate” – not sure it is a real word (google has very few instances of it being used)

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

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declared I have no competing interests.