Reviewer's report

Title: Prognostic and diagnostic value of epithelial to mesenchymal transition markers in pulmonary neuroendocrine tumors

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Reviewer: Teh-Ying Y Chou

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Attempts were made to evaluate by immunohistochemistry the roles of E-cadherin/beta-catenin complex integrity and EMT markers in the diagnosis and outcome prediction of pulmonary neuroendocrine carcinomas. The following issues should be taken care of before acceptance for publication is considered:

Major Compulsory Revisions

1. The interpretation of the immunohistochemistry results is performed by two independent observers. How was the “intra-observer” discrepancy? What was the “inter-observer” discrepancy? When discrepancy in initial immunohistochemistry interpretation occurred, a third observer is provided. How would the discrepancy be solved with the third opinion? The methodology in formulating the final diagnoses should be addressed and discussed in the section of Materials and Methods.

2. In Figure 1, the immunostain of N-cadherin illustrated in 1H showed negative results, however, in the figure legend, it was interpreted positive. Please explain.

3. In Figure 2, the immunostains on neuroendocrine carcinomas were shown to illustrate more cytoplasmic cadherins and beta-catenin staining (indicating loss of E-cadherin/beta-catenin complex integrity) in LCNEC and SCLC. However, in Figure 2 the immunostains in LCNEC or SCLC, when present, are all membranous. Please explain.

4. In this current version, most of the text in the Discussion was to repeat what had been said in the Results. More in-depth discussion on the interpretation pitfalls and clinical applications in immunohistochemistry should be included in the Discussion section.

Minor Essential Revisions

5. Loss of E-cadherin/beta-catenin complex integrity is assigned when at least one marker is not observed in the membrane. In case of loss of membranous beta-catenin, will it go into the nucleus?

6. A few English and grammatical errors need to be corrected.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests