Reviewer’s report

Title: Effect of metastatic site on survival in patients with neuroendocrine neoplasms (NENs). An analysis of SEER data from 2010-2014

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Reviewer: Min Fan

Reviewer's report:

In this study, the authors used the SEER database and identified NENs patients diagnosed between 2010-2014 and assessed the impact of tumor origin and the location of metastasis in survival. I have several concerns.

1. In this study, for Lung NEN patients, the histological grade classification is not suitable. According to the 2015 WHO classification, Lung NEN patients should be classified into typical carcinoid, atypical carcinoid and large cell NEC (LNEC).

2. WHO Classification 2017 of neuroendocrine organ has published. And for pancreatic NEN, NET (according WHO 2017) has to be distinguished in three subcategories according to Ki-67 labelling index: NET G1 <$3\%$; NET G2 3-20% and NET G3 $\geq 20\%$. Never authors distinguish NET according to these strongly validated WHO rules. Actually, Pan-NEN should be divided into well-differentiated Pan-NET (G1, G2 and G3) and poorly differentiated. I suggested that Pancreatic NEN be excluded from this study, because the author might not be able to reclassified them according to the 2017 WHO criteria by using the SEER database. What is the authors' concerns.

3. M stage analysis using data base is very difficult. As written in Collaborative Stage Transition Newsletter (January 19th, 2016), many pM0 may include case with cM1, because pathologists did not assess metastatic site without specimens, and in consistent coding practice and data loss is found. Therefore, many bias can be exist in this study. Moreover, data in this study included many Nx cases.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
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I am able to assess the statistics

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