

Peer Review File

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Reviewer A

1. I would recommend a bit more discussion regarding the conclusion that receiving chemotherapy results in shorter OS. There is a brief statement in both the discussion and conclusion regarding this, however the author should elaborate on limitations and possible explanations given the discordance with other studies. (for example: chemo based on stage ie comparing stages I to stage II and III vs patients with stage II and III who did and did not receive chemo.)

Reply 1: Thank you so much for your comment. Your suggestion has provided us with a valuable direction for enhancing the depth and clarity of our discussion. We appreciate your input and are committed to addressing these points to strengthen the overall quality and validity of our paper. In response to your comments, we carefully reviewed the relevant literature and found that the article's presentation is not rigorous in certain aspects. The results showed that chemotherapy group had a shorter OS, but had no significant effect on patients with LCNEC ($P=0.12$). We describe on page 6, lines 252-253. There were certain limitations that should be noted in our study due to small sample size or heterogeneity. While, Further analysis is not possible at present due to the inaccessible specific content of chemotherapy and radiotherapy, such as the specific dosage of chemotherapy and radiotherapy. Therefore, in the discussion section of the article, we have provided separate descriptions for these aspects. Dresler et al. reported no survival benefits from postoperative chemotherapy, radiation therapy, or both in patients with resected LCNEC (46). We describe on page 8, lines 352-354. In addition, we carefully reviewed the SEER database related literature on LCNEC, and we found that upfront surgery was suggested in the early stages (stage I to IIB), and should also get adjuvant chemotherapy in accordance with small cell lung cancer (SCLC) protocol, according to current treatment recommendations (38, 39). We describe on page 8, lines 334-336. Thanks again for your comment.

Changes in the text: While, patients receiving chemotherapy had a shorter OS than those who did not, but had no significant effect on patients with LCNEC ($P=0.12$). (see Page 6, lines 252-253)

Reviewer B

1. The Background in the Abstract should describe relevant background information. For example, what is known and unknown. While the current one contains only the object. Please modify your abstract.

Reply 1: Thank you so much for your comment. I have made the changes in the

document as per your suggestions.

Changes in the text: Pulmonary large cell neuroendocrine carcinoma (LCNEC) is a rare subtype of breast cancer, with a poor prognosis, Despite its rarity, it is important to gain a better understanding of the epidemiological, clinical, and prognostic features of pulmonary LCNEC. The purpose of this study was to design, construct, and validate a new nomogram for predicting overall survival (OS) in patients with pulmonary LCNEC.

2. Figures and Tables

- Figures should be cited **consecutively** in the text and numbered in the order in which they are discussed. Therefore, Figure 5B should be cited before Figure 5C, unless Figure 5 is cited as a whole before. Please check through and revise.
- Please provide **an editable version of Figure 1** as a stand-alone **WORD/PPT** file, so that the editor can slightly and properly adjust the lines and structures, and text during the editing (Note: use **arrows** as the connections among boxes).
- **All abbreviations** in figures and legends should be explained. “ICD-O-3” “AJCC” “NA” “SEER” in Figure 1 for example. Please check all abbreviations and provide the full names in the corresponding legends.
- The numbers in Figure 2A are not clear enough. Please modify.

12 —

10 —

4 —
3 —
3 —

- There is no “OS” in Figure 2 while it is explained in the legend. Please check.

OS, overall survival. ←

- Please check whether it should be **3-year, and 5-year in Figure 3.**

3-years Survival Probability

5-years Survival Probability

- Please check the **y-axis of Figure 4**, whether it should be “Actual 3- and 5-year survival rate”.

Actual 5- and 5 year survival rate

- Please also check the **x-axis of Figure 4**. Whether it should be “3- and 5-year survival rate”?

Predict 3- and 5 year survival rate

- Please check whether it should be “three-year” “five-year” in Figure 5.
 - three.year.survival.probability.TNMstage
 - three.year.survival.probability.Nomogram
- Please provide description for the x-axis in **Figures 6A, 6C** and indicate the meaning of “FP” “TP” in the legend.
- There is a spelling mistake in **Figure 7A**.

+ 0-59years
+ 60+yeaas

- The “unknow” in **Figure 7** should be “**unknown**”. Please check and revise.

+ no/unknow

- Please provide a summarized legend for figure 8

Fig. 8. Time-dependent ROC curve analysis of the nomogram for the 3 and 5 years in the training cohort (A) and the validation cohort (B). Kaplan-Meier plots compare overall survival between patients in low and high-risk groups in the training cohort (C) and in the validation cohort (D).

- Please check whether it should be 3-year, 5-year in **Figure 4A, 4B** and **Figure 8A, 8B**.

— dev_3 year
— dev_5 year

- Please add **unit for Time** in the x-axis of **Figure 8C, 8D**.
- Please add **unit for Age** in **Tables 1-3**.
- The “unknow” in Tables 1-3 should be “**unknown**”. Please check through and revise.
- The data mentioned in the following sentence is inconsistent with **Table 1**. Please recheck.

“Besides, we observed that the brain was the most common distant metastasis organ, accounting for 17.1% of patients, followed by bone (15.7%) , liver (15.2%), and lung (12.9%).”

Lung metastasis	
no/unknow	1677 (90.0)
yes	187 (10.0)

- In all tables, please uppercase the first letter of each column.

Reply 2: Thank you so much for your comment. The formats of both the figure and the table have been revised as per the requirements.