

Round-1:

Oct. 30, 2020

Manuscript NO.: 59568

Title: Primary lung cancer with radioiodine avidity: A thyroid cancer cohort study

### **Responses to Reviewer's and Editorial Office's comments**

#### **Reviewer 1:**

Specific Comments to Authors: In this article, the authors did a lot of screening, reporting a rare case of primary lung cancer with RAI uptake after thyroid cancer surgery. They also analyzed the possible mechanisms. These data have some meaning to clinical practice. Only two explanations are needed: 1.LINE195-198: The histologic types of these cancers were Adenocarcinoma (N = 27) , non-small Cell Carcinoma (N = 3) , Small Cell Carcinoma (N = 1) , adenosquamous lung carcinoma (n =1), and poorly-differentiated lung carcinoma (N = 1) . Please explain why non-small cell lung carcinoma does not include adenocarcinoma, adenosquamous carcinoma and poorly-differentiated carcinoma? What are the criteria for such pathological classification? 2. Line206-208: The histological types of lung cancer were Adenocarcinoma in eight patients and non-small-cell lung carcinoma in one patient. Please explain why non-small cell lung carcinoma does not include adenocarcinoma? What are the criteria for such pathological classification?

#### **Response:**

We acknowledge the reviewer for very helpful comments. We have reviewed these 3 cases of non-small cell lung carcinoma (NSCLC) with additional immunostaining studies. Two of them can be further classified as squamous cell lung carcinoma, since both were positive for P63 and negative for TTF-1. The remaining one lung cancer was classified as NSCLC-not otherwise specified (NOS) owing to insufficient tumor sample for immunostaining. We have clarified these points in the revised draft (lines 174, 176-178).

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing

needs.

**Response:**

This draft was reviewed and revised by Crimson Interactive INC.

The grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability was edited (lines: 9-12, 50, 60, 67-68, 70, 92, 96, 99, 103, 109, 114-116, 124, 134, 136, 140-143, 147, 154, 162, 179-180, 193, 201, 226, 236, 245, 249, 251, 259, 275, 279, 281, 288-290, 299, 306-307, 309-310, 313, 318, 323-324, 328, 536).

**EDITORIAL OFFICE'S COMMENTS:**

Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the Primary lung cancer with radioiodine avidity. The topic is within the scope of the WJCC. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: In this article, the authors did a lot of screening, reporting a rare case of primary lung cancer with RAI uptake after thyroid cancer surgery. They also analyzed the possible mechanisms. These data have some meaning to clinical practice; and (3) Format: There are 2 tables and 2 figures. A total of 38 references are cited, including 7 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade B. A language editing certificate issued by Melody was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, written informed consent and the Institutional Review Board Approval Form. Please provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by Chang Gung Memorial Hospital and US National Institutes of Health. The topic has not previously been published in the WJCC. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

**Response:**

We appreciate the Editorial Office for these very helpful comments. The Conflict-of-Interest Disclosure Form, Copyright License Agreement, Funding agency copy of grant approval documents, the Figures using PowerPoint, and Table files using Word were all uploaded. The “article highlights” section was included at the end of the main text (lines 340-377).

Round-2:

Nov. 06, 2020

Manuscript NO.: 59568

Title: Primary lung cancer with radioiodine avidity: A thyroid cancer cohort study

Responses to Reviewer's comments

Reviewer 1: I don't think the authors cited the appropriate reference (R16) to support "the criteria pathological classification" in the file of "Answering reviewers" and in the main text. The authors did not answer the reviewer's concerns point-by-point. No response was found about Query2 from review in the file of "Answering reviewers".

Response: We appreciated the reviewer's for further comments on our draft. The review and revision process allowed us to improve the quality of this manuscript significantly. We have addressed every point raised by the reviewer and revised the draft accordingly, below.

Query 1. I don't think the authors cited the appropriate reference (R16) to support "the criteria pathological classification" in the file of "Answering reviewers" and in the main text. LINE195-198: The histologic types of these cancers were Adenocarcinoma (N = 27) , non-small Cell Carcinoma (N = 3) , Small Cell Carcinoma (N = 1) , adenosquamous lung carcinoma (n =1), and poorly-differentiated lung carcinoma (N = 1) . Please explain why non-small cell lung carcinoma does not include adenocarcinoma, adenosquamous carcinoma and poorly-differentiated carcinoma? What are the criteria for such pathological classification?

Response: According to "The 2015 World Health Organization Classification of Lung Tumors (Travis WD et al. J Thorac Oncol. 2015;10:1243-1260)", non-small cell lung carcinoma (NSCLC) includes adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma and poorly-differentiated carcinoma. We have clarified this point in revised draft (lines 173-179) and revised Figure 1. This new reference was included in the revised draft (R16), and the original R16 was deleted due to inappropriate citation. We regret for the mistake.

Query 2. Line206-208: The histological types of lung cancer were Adenocarcinoma in eight patients and non-small-cell lung carcinoma in one patient. Please explain why non-small cell lung carcinoma does not include adenocarcinoma? What are the criteria

for such pathological classification?

Response: In this study, nine of 33 patients received RAI scan within 1 year prior to the histological diagnosis of lung cancer. All of these 9 patients had non-small cell lung cancers (NSCLC), including eight patients had adenocarcinoma and one patient had non-small cell lung cancer-not otherwise specified (NSCLC-NOS). The classification of lung cancers was according to the 2015 World Health Organization Classification of Lung Tumor (Travis WD et al. J Thorac Oncol. 2015;10:1243-1260). We have clarified these points in revised draft (lines 184-186).