Peer review file

Article information: https://dx.doi.org/10.21037/acr-21-35

Review comments

Comment 1: Page 5 line 83-84 – to say NUT carcinoma is a subtype of SCC and then to subsequently state it can be confused with SCC. This may confuse the reader. Perhaps it is best to say it may not be appreciated or identified.
Reply 1: I agree with the reviewer's comments.
Changes in the text: We have modified our text as advised

Comment 2: Did the patient have a history of smoking? You do go on to mention that most patients are non-smokers so it would be important to clarify if this patient is typical for a NUT patient.
Reply 2: We reviewed the patient's chart carefully and found that he was a non-smoker
Changes in the text: We have added the asked information

Comment 3: Page 7, line 121 – You should use the drug name paclitaxel instead of 'taxol'
Reply 3: I agree with reviewer's comment
Changes in the text: We have modified our text

Comment 4: Page 7, line 122 – "the patient also received a total of 6000cGy of radiation starting:". Has this sentence been cut in half?
Reply 4 : The word "starting" was extra, so removed it
Changes in the text: We modified our text
Comment 5: Page 7, line 125 – What is a significant response? If this could be put into partial response or complete response by RECIST criteria that would be more appropriate.
Reply 5: The response type has been defined as per reviewer's request
Changes in the text: We have added the asked information

Comment 6: How do you reconcile in this case that 2 independent biopsies favoured adenocarcinoma when NUT carcinoma typically appears to be squamous cell carcinoma? Was NUT IHC performed on any of the specimens? Was the resected intracanial specimen consistent with adenocarcinoma or squamous cell carcinoma? Have all the specimens been compared?

This is an important point as you state NUT carcinoma is a subtype of squamous cell carcinoma however no biopsy specimen histologically appeared to be a squamous cell carcinoma.

Reply 6: For the first 2 biopsies (right paratracheal LN and left arm muscle biopsy) IHC revealed weak TTF-1 positive staining, lack of p40 staining and absence of evidence of keratinization, therefore initial diagnosis of poorly differentiated adenocarcinoma of the lung was made but once next-generation sequencing revealed the presence of a NUTM1-BRD4 fusion, it confirmed the diagnosis of NUT midline carcinoma. No NUT specific IHC was performed. For the last biopsy (brain lesion) IHC for NUT was performed that was positive and it was confirmed by NGS.

Changes in the text: Some modification done in the text

Comment 7: Page 9 line 161 – I wouldn't mention palliation here as the patient has subsequently gone on to receive further active lines of palliative treatment (radiotherapy and chemoimmunotherapy). However, if by palliation you mean palliative intent therapy this is not consistent as palliative systemic therapy has been used since molibresib was commenced.

Reply 7: Palliation implied "palliative intent" but I agree with the reviewer and removed palliative here since patient had received palliative intent treatment before this paragraph.

Changes in the text: Some modification done in the text

Comment 8: Page 11 line 222 – this patient received radiotherapy to their intramuscular lesion, their brain metastases and their pulmonary disease. How was the response to radiotherapy at these sites captured? PR? SD? PD?

Reply 8: I agree with the reviewer. All the responses have been added as per RECIST criteria.

Changes in the text: We have added the asked information

Comment 9: Page 12 line 231 – you state the patient has a "disease free period". Does this mean they had no radiologically detectable malignancy (i.e. had a complete radiological response to chemoradiotherapy)? Appropriate terminology may clear up this confusion.

Reply 9: I agree with reviewer and have changed it to "partial response"

Changes in the text: Some modification done in the text

Comment 10: Page 12 line 235 – Do you mean progression or recurrence? These are not the same thing.

Reply 10: Given that patient had only partial response to the initial therapy, I would consider it progression.

Changes in the text: Only clarification done here

Comment 11: Page 12 line 239 – "generally resistant to radiation". The paper you cite here does not really give any evidence or data to support this statement beyond their opinion. I would not consider this a high level of supporting evidence.

Reply 11: I agree with the reviewer therefore I have removed it.

Changes in the text: Some modification done in the text

Comment 12: Page 18 line 328 - given you are commenting on hilar lymphadenopathy it may be more appropriate to include soft tissue rather than lung windows on the imaging displayed.

Reply 12: The suggested window has been updated

Changes in the text: Modification done in the figure