

Advances in multimodal treatment for stage IIIA-N2 nonsmall cell lung cancer

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Handling editor:

Michal Heger

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Review timeline:

Received: 30 September, 2020 Editorial decision: 9 November, 2020 Revision received: 9 Dec, 2020 Editorial decision: 27 January, 2021 Revision received: 14 February, 2021 Editorial decision: 18 March, 2021 Published online: 16 April, 2021

1st Editorial decision 09-Nov-2020

Ref.: Ms. No. JCTRes-D-20-00109 ADVANCES IN MULTIMODALITY TREATMENT FOR STAGE IIIA NSCLC Journal of Clinical and Translational Research

Dear Ms Montemuiño Muñiz,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below. We kindly ask you to pay particular attention to reviewer # 2 and accommodate the reviewer's comments to a maximum extent. Narrative structure and language use should comply with academic standards, as indicated overtly in our author guidelines.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the



reviewers to rapidly verify all changes made.

Your revision is due by Dec 09, 2020.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger Editor-in-Chief Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: Good review, entertaining, comprehensive and easy to read.

In 3.2. Surgical techniques, line 33. "The median sensitivity is 0.99, with a NPV of 0.96 and a 4% false negative rate". As a sugerence, maybe you could use the percentage as it is what you use throughout the text.

In 7. Immunotherapy and targeted therapies. Line 31. Consider, "...patients WITH locally-advanced disease."

Review references with missing authors.

Reviewer #2: This is a very well written review article describing the advances in multimodality treatment for stage IIIA NSCLC. However, there are some problems to be further improved as well:

- 1. The logic of the article needed further improved. Stage IIIA NSCLC is a highly heterogeneous group of diseases. According to a complete staging examination before treatment, stage IIIA NSCLC can be divided into the following three groups: operable, possibly resectable and unresectable. The treatment of IIIA NSCLC can be elaborated from the above three groups.
- 2. The role of postoperative radiotherapy (PORT) in resected stage IIIA-N2 non-small cell lung cancer (NSCLC) patients remains controversial. In some non-randomized analyses, PORT appears to improve survival significantly as an adjunct to postoperative chemotherapy. However, a recently prospective randomized phase III Study LungART showed that PORT has not been shown to significantly improve DFS or OS. This article can further t elaborated this question properly.
- 3.The knowledge in this manuscript focus on neoadjuvant therapies (included preoperative chemotherapy followed by Surgery versus surgery alone, preoperative concurrent chemoradiation therapy versus preoperative chemotherapy, preoperative concurrent chemoradiation therapy versus definitive concurrent chemoradiation, preoperative targeted therapies versus preoperative chemotherapy, preoperative immunotherapy versus preoperative chemotherapy, etc.) are not sufficient. The author can dig deeper into the current study before the article can be accepted.



4. There is at least one error in the manuscript, such as, in references, 3 and 54. Please check the manuscript carefully.

Authors' response

Responses to Reviewers' Comments

Dear Prof. Michal Heger, PhD.

Thank you for giving me the opportunity to submit a revised draft of my manuscript titled "Advances in multimodality treatment for stage IIIA-N2 NSCLC" to *Journal of Clinical and Translational Research*. We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on our manuscript. Each comment has been carefully considered point by point and responded. We have <u>underlining</u> the changes within the manuscript.

Comments from Reviewer #1

Comment 1: "In 3.2. Surgical techniques, line 33. "The median sensitivity is 0.99, with a NPV of 0.96 and a 4% false negative rate". As a sugerence, maybe you could use the percentage as it is what you use throughout the text".

Response: Thank you for this suggestion. We Agree. We have, accordingly, proceeded to change (section: 3.2 Surgical techniques).

Comment 2: "In 7. Immunotherapy and targeted therapies. Line 31. Consider, "...patients WITH locally-advanced disease".

Response: We agree and have proceeded to change (Section 8.1 Targeted therapies)

Comment 3: "Review references with missing authors".

Response: Both reviewers have agreed on this assessment and we agree with the suggestion. We have proceeded to correct (section: References).

Comments from Reviewer #2

Comment 1: "The logic of the article needed further improved. Stage IIIA NSCLC is a highly heterogeneous group of diseases. According to a complete staging examination before treatment, stage IIIA NSCLC can be divided into the following three groups: operable, possibly resectable and unresectable. The treatment of IIIA NSCLC can be elaborated from the above three groups".

Response: Thank you for this suggestion. We agree. However, the objective of this review was potentially-resected IIIA-N2 NSCLC. We have to proceeded change (Section: Title, Abstract, Introduction and conclusions).



Comment 2: "The role of postoperative radiotherapy (PORT) in resected stage IIIA-N2 non-small cell lung cancer (NSCLC) patients remains controversial. In some non-randomized analyses, PORT appears to improve survival significantly as an adjunct to postoperative chemotherapy. However, a recently prospective randomized phase III Study LungART showed that PORT has not been shown to significantly improve DFS or OS. This article can further t elaborated this question properly".

Response: We agree with the reviewer's comment and we have incorporated your suggestion throughout the manuscript (Section: 6. Role of postoperative radiotherapy).

Comment 3: "The knowledge in this manuscript focus on neoadjuvant therapies (included preoperative chemotherapy followed by Surgery versus surgery alone, preoperative concurrent chemoradiation therapy versus preoperative chemotherapy, preoperative concurrent chemoradiation therapy versus definitive concurrent chemoradiation, preoperative targeted therapies versus preoperative chemotherapy, preoperative immunotherapy versus preoperative chemotherapy, etc.) are not sufficient. The author can dig deeper into the current study before the article can be accepted".

Response: We appreciate the reviewer's correction. We have to proceeded to update therapies in IIIA-N2 NSCLC (Section: 4. Role of traditionally neoadjuvant treatment: chemotherapy and chemoradiotherapy, 8.1. Targeted therapies, 8.2 Immunotherapy, Table 2, 4, 5 and 6).

Comment 4: "There is at least one error in the manuscript, such as, in references, 3 and 54. Please check the manuscript carefully".

Response: Both reviewers have agreed on this assessment and we agree with the suggestion. We have proceeded to correct (section: References).

We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

2nd Editorial decision 27-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00109R1 ADVANCES IN MULTIMODALITY TREATMENT FOR STAGE IIIA-N2 NSCLC Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-



by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Feb 26, 2021.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger Editor-in-Chief Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for resubmitting your paper, which has sufficiently taken into account the reviewers' comments.

The last stage of your article processing boils down to language, which still needs considerable improvement.

Please ensure that the use of the English language conforms to academic English, as is stipulated in the author guidelines. JCTR cannot publish articles written in substandard English.

Feel free to contact the editorial office if you need help with language editing.

Thank you and kindest regards,

Michal Heger Editor

3rd Editorial decision 18-Mar-2021

Ref.: Ms. No. JCTRes-D-20-00109R2 ADVANCES IN MULTIMODAL TREATMENT FOR STAGE IIIA-N2 NON-SMALL CELL LUNG CANCER (NSCLC) Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.



You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger Editor-in-Chief Journal of Clinical and Translational Research

Comments from the editors and reviewers: