Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-1029

REVIEWER A

Comment 1: What is the rationale for testing liquid biopsy since tissue was available for all patients (they have been tested for EGFR by RT-PCR)? A comparison between tissue and plasma would have been interesting (although not novel).

Reply 1: Our group was able to access next-generation sequencing via liquid biopsy through a financial requirement access, which did not include tissue evaluation by NGS.

Changes in the text: We have modified our text as advised (see Page 8, lines 139-140)

Comment 2: Since one of the objectives was to determine the characteristics of Mexican patients, the data obtained must be compared to available data from different countries/ethnicities.

Reply 2: A comparison with European and Asian populations was added to the discussion, highlighting the main genetic alterations found in these population groups.

Changes in the text: We have modified our text as advised (see Page 17, lines 346-350)

Comment 3: The authors should indicate in the title that liquid biopsy was tested by NGS, and that the patients were Mexican.

Reply 3: We have modified our title of the manuscript to read as follows “Mutation profile in liquid biopsy tested by NGS in Mexican patients with Non-Small Cell Lung Carcinoma and its impact on survival.”

Changes in the text: We have modified our title as advised (see Page 01, lines 3-5)

Comment 4: An EGFR mutation was detected in 24 patients. The list of these alterations must be provided, and the authors must discuss why they were not detected in the tissue. This is important because some of them might be not eligible to EGFR inhibitors.

Reply 4: The complete list of mutations affecting the EGFR gene has been added in a table included in the supplementary appendix, along with a comment in the discussion section regarding these alterations.

Changes in the text: We have modified our title as advised (see Page 18, lines 374-376 and Page 19, lines 379-383)

Comment 5: The name and characteristics of the RT-PCR test used for EGFR are mandatory.

Reply 5: The mutations were obtained by Idylla™ real-time PCR based molecular testing system **Catalog number: P1010**, using cartridges Idylla™ EGFR Mutation Test **Catalog number: A0060/6**

Changes in the text: We have modified our title as advised (see Page 08, lines 148-151)

REVIEWER B

Comment 1: An extensive English language revision is required.

Reply 1: Our team performed an extensive language revision

Changes in the text: Multiple changes in the text

Comment 2: The objectives described in the section 1.3 are not in line with study endpoints; you analyzed OS and PFS of advanced mutated adenocarcinoma NSCLC patients, not for all stages and non-mutated NSCLC.

Reply 2: All patients included in our protocol had a diagnosis of advanced-stage adenocarcinoma, so we will add it to the objectives.

Changes in the text: We have modified our text as advised (see Page 7, lines 131-132)

Comment 3: Considering that patients included in the study had a cancer tissue biopsy, why did you perform NGS on liquid biopsy? The tissue specimens were not enough? This aspect should be detailed and clarified.

Reply 3: Our group was able to access next-generation sequencing via liquid biopsy through a financial requirement access, which did not include tissue evaluation by NGS.

Changes in the text: We have modified our text as advised (see Page 8, line 137-138)

Comment 4: Line 149 should be revised (e.g. "The genes explored are shown in table 1").

Reply 4: We deleted line 149, the reference to the table was added to the text

Changes in the text: We have modified our text as advised (see Page 08, line 156)

Comment 5: Results section should only include a description of study results; any comments must be placed in the discussion section (lines 203-210).

Reply 5: We made revisions to our manuscript, relocating the highlighted sections to the discussion, and retaining only the results.

Changes in the text: We have modified our text as advised (see Page 11, lines 214-221 and page 17, lines 341-344)

Comment 6: BRAF discussion in lines 289-290 should be improved with other recent literature evidence, doi: 10.3390/biomedicines11010153.

Reply 6: The corrections were made to the highlighted lines, adhering to the recommended bibliographic guidance

Changes in the text: We have modified our text as advised (see Page 15, lines 301-307)

Comment 7: Number at risk table should be added for both PFS and OS in figure 3 and 4.

Reply 7: We do not understand what is being requested in this question; we are uncertain whether it pertains to the number of patients in relation to temporality.

Changes in the text: No changes in figures.

Comment 8: 95% CI is mandatory for the Hazard Ratio of multivariable analysis in both table 3 and 4, so it must be added.

Reply 8: We re-performed the multivariable analysis of the data in our manuscript, and it was confirmed that there was an error in the calculation of Hazard Ratio. As a result, we have rectified the manuscript.

Changes in the text: The requested changes have been made in tables 3 and 4.