Reviewer #1:

The authors assessed KRAS mutation status in patients with metastatic (stage IV) non-small cell lung cancer (NSCLC) as a positive predictor of immune checkpoint blockade therapy and a negative predictor of platinum-based two-agent chemotherapy and general OS in stage IV NSCLC. This manuscript is interesting and clinically informative. The reviewer has the following concerns to prompt the manuscript for publication.

We thank the reviewer for the positive assessment of our manuscript.

The introduction describes the study background well, however, "two inhibitors efficiently targeting mutant KRAS-G12C have been developed but the clinical efficacy is yet to be determined in ongoing trials [23-27]."
This statement is not a particularly appropriate summary, as it is important to note that the KRAS G12C inhibitor AMG 510 has been approved for clinical use. Despite the fact that potential resistance to this class of molecules has emerged (PMID: 34864132). Hence, the authors should clearly describe here the KRAS G12C inhibitors that are already available for clinical use and point out that possible resistance also exists. These indications and citations are necessary.

We thank the reviewer for pointing this out. Indeed, during the course of our study, the first KRAS-G12C inhibitor, have been approved by the FDA as a second-line of treatment, although, approval is still pending in Europe/Sweden. We have now amended the introduction as follows:

“More recently, several inhibitors specifically binding mutant KRAS-G12C have been investigated in clinical trials, among these Sotorasib is the first treatment to gain approval for adults with NSCLC whose tumors have KRAS-G12C mutation as second-line therapy [23-27]. However, like other SMKIs, a heterogenous pattern of resistance to KRAS-G12C inhibition has already been observed [28,29].”

The necessary clinical ethics approvals are required to be uploaded.

We have now clarified and added the following statement regarding the ethical numbers at the end of the manuscript. This ethical number is also mentioned is the method section.

“**Institutional Review Board Statement**

Approval from the Swedish Ethical Review Authority (Dnr 2019-04771) was obtained prior to study commencement.”

Univariate and multivariate analysis methods need to be progressively clarified.

Thank you for the comment. We have now clarified in the manuscript the univariate and multivariate analysis methods. We also have included multivariate analyses performed in Supplementary Table 3.

The graphs should preferably be presented in vector form. Figure 4A is vague and therefore the IHC results are unclear.

For the revised version, we have provided higher resolution figures and we hope they now look clear.

We believe that after addressing all the comments and suggestions from the reviewer, our manuscript has now significantly improved, and we hope the reviewer agrees with us that it is now suitable for publication.