

Title: Oncogenic driver mutations in NSCLC: past, present and future.

Authors: Mathieu Chevallier, Maxime Borgeaud, Alfredo Addeo and Alex Friedlaender

Answers to Reviewer #1 (received 02.02.2021)

1. In this manuscript, the authors mentioned acquired secondary mutation such as EGFR T790M that can lead to resistance to targeted therapy. It is unclear whether the second mutation is pre-exist before targeted therapy or drug treatment generates this secondary mutation.

Thank you for your constructive remark. A sentence was added to specify that the presence of a mutated clone -such as T790M- before treatment was present, then selected under TKI treatment.

2. It would be much better for readers to understand if the authors can create a table to summarize current targeted therapies for NSCLC patients based on driver mutation status.

A table was created for this purpose.

3. Fig.1 is not well presented. For example, KRAS G12C is shown under KRAS section. It is unclear what percentage for KRAS G12C. Additionally, other genes do not show specific point mutations. It should be consistent for all genes. Furthermore, unknown/no mutation is 27%. The word “No mutation” should be removed because we do not know the real answer.

We apologize for the lack of clarity of this figure, modifications have been made.

4. Under “RET” section, “RErranged” is one spelling error.

Thank you for pointing this spelling error. This was corrected in the manuscript.

5. How is ALK activated? Please explain.

An explanation has been added. Thank you.