Peer Review File

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Reviewer A

This article reviews therapeutic development of BRAFmut-NSCLC and their characteristics. It is well organized and may be instructive for the readers. However, there are a few points of concern, which are described below.

1. **Although the authors titled the article 'Encorafenib and Binimetinib for the treatment of metastatic BRAF mutant non-small cell lung cancer', I consider this inappropriate, as the article contains only a small amount of data on Encorafenib and Binimetinib.**

We thank the reviewer for this comment. Indeed, we have changed the title of our manuscript to "The evolving treatment landscape for BRAF-mutated non-small cell lung cancer" to comply with their suggestion.

2. **Drug approval and recommendations for first-line treatment vary from country to country and region to region, therefore it is misleading to uniformly state "For other oncogenic drivers in NSCLC, such as BRAF, HER2, MET, RET, ROS1, KRAS and NTRK, targeted therapies are approved in later lines and / or on the basis of single-arm studies" is misleading. To the best of my knowledge, for example, the NCCN guidelines or the Japanese Lung Cancer Society guidelines recommends targeted therapy as the first-line treatment for BRAFmut-NSCLC.**

We appreciate this comment from the reviewer and have edited this sentence of our manuscript. The new text reads: "For other oncogenic drivers in NSCLC, such as BRAF, HER2, MET, RET, ROS1, KRAS and NTRK, targeted therapies are also approved on the basis of single-arm studies".

3. (In Fig1) Is it true that BRAF non-V600E is more common in early-stage NSCLC? Provide the data to support it.

We thank the reviewer for this comment. We have referenced Litvak et al. in the accompanying text to support the increased likelihood of non-V600E BRAF mutations being identified in NSCLC that were diagnosed at early stages, whereas V600E BRAF mutant cancers are more likely to be found in cancers diagnosed that were stage IV at the time of diagnosis.

We've added the following sentence to the text in order to clarify this point:

"Although both BRAF V600 and non-V600 mutant NSCLC are diagnosed at all stages, BRAF V600 are more likely to be diagnosed at Stage IV, whereas non-V600 are more likely to be diagnosed at Stages I-II".

We have also made a slight modification to the figure to help clarify this point.

Reviewer B

This is a nice and well written editorial commentary.

We thank the reviewer for the comment stating that “This is a nice and well written editorial commentary”.

Here below only some minor comments:

1. **"Oncogene-driven non-small cell lung cancer (NSCLC) represents a subgroup of lung cancers that are potentially actionable with targeted therapies" --> "Oncogene-driven non-small cell lung cancer (NSCLC) represents a subgroup of lung cancers that harbors specific molecular activations, and is responsive to targeted therapies"**

We thank the reviewer for this comment and have incorporated their suggestion into the text verbatim.

2. **I would not go into details in the paragraph "Implications for non-V600 BRAF mutant NSCLC" (I would rather remove the paragraph itself). I agree that this is a relevant aspect of BRAF-mutant NSCLC, but as the topic of the editorial is PHAROS and this latter focuses on BRAF V600, the non-V600 part could be unmet need could be mentioned in the final paragraph as a question to which we need to answer with clinical indications.**

We thank the reviewer for this comment but we chosen not to incorporate it. As the reviewer points out, this is a very relevant aspect of BRAF-mutant NSCLC, and while the topic of the editorial is primarily focused on the PHAROS trial, the fact that non-V600 BRAF mutant cases were excluded from this trial and that non-V600 BRAF mutations represent the most frequent type of BRAF mutations in NSCLC, highlights that there exists a gap in our knowledge for how to treat NSCLC with non-V600 BRAF mutations. We have modified our title to “The evolving treatment landscape for BRAF mutant NSCLC”, therefore the title encapsulates a broader perspective on all BRAF mutant NSCLC.

We feel strongly that the included paragraph describes an important nuance in the management of BRAF mutant NSCLC. Indeed, non-V600 BRAF mutations comprise up to 50% of BRAF mutations in NSCLC but are not sensitive to the approved BRAF and MEK inhibitor combinations. We feel as though a brief discussion on emerging strategies to exploit non-V600 BRAF mutations for therapeutic benefit is relevant for this commentary.

We assure that the authors have completed and submitted the conflict-of-interest forms provided. None of the authors of this manuscript are serving as a current Editorial Team member (such as Editors-in-Chief, Editorial Board Member, Section Editor) for this journal. We also assure that all figures/tables/videos in this manuscript are original.