Peer Review File

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- Reviewer 1
  - **Comment 1:** In line 76th: please correct ATLA1L with ALTA1L
  - **Reply 1**: we changed the name of the trial accordingly (Page 4, Line 5)
  - **Comment 2:** In RET rearrangement section, the addition of the following reference, underlining the role of RET fusions as predictor of unresponsiveness to ICIs, should be useful: *Baglivo, S., Ludovini, V., Moretti, R. et al. RET Rearrangement as a Predictor of Unresponsiveness to Immunotherapy in Non-Small Cell Lung Cancer: Report of Two Cases with Review of the Literature. Oncol Ther (2020). https://doi.org/10.1007/s40487-020-00116-2*.
  - **Reply 2**: We added the reference as suggested among the clinical evidence in RET section (Page 7, Line 42)
  - ***Comment 3:*** *Considering that the authors have correctly included* 'Emerging oncogene rearrangements' *in a separated paragraph, I would suggest the implementation of more details about the upcoming fusions. 1) Very limited data about NTRK rearrangements and immunotherapy implication are available (TMB and PD-L1 levels similar to not oncogene addicted subgroups and co-existence with STK11 mutations).* Skoulidis F, Goldberg ME, Greenawalt DM, et al. STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Lung Adenocarcinoma. Cancer Discov 2018;8:822-35. 2) *The same for NRG1 fusion-positive tumors.* Duruisseaux M, Liu SV, Han JY, et al. NRG1 fusion-positive lung cancers: Clinicopathologic profile and treatment outcomes from a global multicenter registry. J Clin Oncol 2019;37:9081. 3) *About FGFR alterations in lung cancer, the paper by* Qin et al. *includes TMB data.*
  - **Reply 3**: We accepted all suggestions and expanded the "Emerging oncogene rearrangements" section accordingly (Page 8, Lines 26-34).
- Reviewer 2
  - **Comment 1**: My only suggestion is to add among the clinical evidences the following real-world study (Cortellini A, Tiseo M, Banna GL, et al. Clinicopathologic correlates of first-line pembrolizumab effectiveness in patients with advanced NSCLC and a PD-L1 expression of ≥ 50% [published online ahead of print, 2020 May 30]. Cancer Immunol Immunother. 2020;10.1007/s00262-020-02613-9. doi:10.1007/s00262-020-02613-9), just because it provide one more evidence of a somehow less clinical activity of single agent checkpoint inhibitors in oncogene addicted NSCLC patients, including ALK positive ones.
  - **Reply 1**: Unfortunately, we have to reject the suggestion of the Reviewer. The real-world study by Cortellini A, Tiseo M, Banna GL, et al. collected 1026 NCLC patients with high PD-L1 expression (>50%) who underwent first line treatment with Pembrolizumab. It furnished many useful information for clinical practice, but, according to supplementary Table 1 ("Patients characteristics"), no certain ALK positive NSCLC were included in the enrolled

population [ALK wild type 942 (91.8%), ALK unknown 84 (8.2%), ALK positive 0 (0%)]. Therefore, the abovementioned study does not provide more evidence about less clinical activity of checkpoint inhibitors in the population under examination in our review.