Topics: cfNA (Circulating free nucleic acid)
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Feasibility of *BRAF* mutations testing in Non-Small Cell Lung Cancer on Liquid biopsy samples: focus on basal setting.

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Summary: The analysis of circulating tumor DNA extracted from plasma may be a reliable tool to assess v-Raf murine sarcoma viral oncogene homolog B (*BRAF*) mutational status in advanced stage non-small cell lung cancer (NSCLC) patients naïve to any treatment, in roder to administrate targeted therapies.

Introduction: Despite a limited number (1.5-3.0%) of non-small cell lung cancer (NSCLC) patients harbor *BRAF* mutations, international guidelines strongly recommend the identification of *BRAF* exon 15 pV600E in order to administrate targeted therapy regimens (dabrafenib plus trametinib).[1-3] Thus, when tissue is not available, liquid biopsy may represent a viable option for *BRAF* mutational assessment.

Goals: Our aim is to investigate the feasibility to perform BRAF mutational assessment on ctDNA extracted from plasma of advanced stage NSCLC patients naïve to any treatment by adopting an ultradeep next generation sequencing (NGS) approach.

Hypothesis: Advanced stage NSCLC naïve to any treatment with BRAF exon 15 p.V600E point mutations detected on ctDNA extracted from plasma may benefit from the administration of targeted therapy regimens.

Materials and methods: We have retrospectively retrieved from our internal archive, 196 NSCLC blood samples analyzed by an ultradeep NGS approach from January 2016 and December 2018.

Ethical aspects: All samples were handled in compliance with the Helsinki Declaration.

Results: Overall, 6 (3.1%) out of 196 patients harbored a *BRAF* point mutation in exon 11 or 15. The actionable BRAF exon 15 p.V600E was detected in 2 (33.3%) out of 6 instances. Of note, in one of these patients a concomitant *EGFR* exon 19 p.E746_A750del was identified.

Discussion: Our data underlined the technical feasibility of *BRAF* mutation assessment in ctDNA extracted from plasma of advanced stage NSCLC patients naïve to any treatment.

Conclusions and recommendations: Ultradeep NGS approach represents a robust and valid analytical tool to assess *BRAF* mutational status on ctDNA extracted from plasma of advanced stage NSCLC patients naïve to any treatment. Further investigation are required to better define its clinical usefulness in the treatment decision algorithm.

Bibliographic references:

1. Planchard D, Besse B, Groen HJM, et al. Dabrafenib plus trametinib in patients with previously treated BRAF(V600E)-mutant metastatic non-small cell lung cancer: an open-label, multicentre phase 2 trial. Lancet Oncol. 2016;17:984-993.

2. Planchard D, Smit EF, Groen HJM, et al. Dabrafenib plus trametinib in patients with previously untreated BRAFV600E-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. Lancet Oncol. 2017;18:1307-1316.

3. Kalemkerian GP, Narula N, Kennedy EB, Biermann WA, Donington J, Leighl NB, Lew M, Pantelas J, Ramalingam SS, Reck M, Saqi A, Simoff M, Singh N, Sundaram B. Molecular Testing Guideline for the Selection of Patients With Lung Cancer for Treatment With Targeted Tyrosine Kinase Inhibitors: American Society of Clinical Oncology Endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline Update. J Clin Oncol. 2018;36:911-919.