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The role of circulating tumor DNA to predict mutant allelic fraction evolution in non-small cell lung cancer patients: a mathematical model.

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Summary: The analysis of circulating tumor DNA (ctDNA) extracted from plasma of advanced stage non-small cell lung cancer (NSCLC) patients is a non-invasive, dynamic and repeatable tool not only as predictive for responsiveness to targeted therapies, but also to monitor tumor clonal evolution through the evaluation of the mutant allelic fraction (MAF).

Introduction: In advanced stage NSCLC patients, liquid biopsy represents a non-invasive, dynamic and repeatable advice for the assessment of clinically relevant biomarker molecular status and to monitor clonal evolution under targeted treatment administration.[1-3] In this setting, the evaluation of MAF, that is the percentage of mutant alleles in a given locus, may play a fundamental role.

Goals: Our aim is to generate a mathematical model able to describe MAF evolution under targeted treatment pressure in advanced stage NSCLC patients.

Hypothesis: MAF evolution, evaluated through ctDNA serial sampling, may be an useful tool to monitor tumor clonal evolution and to predict responsiveness or resistance to targeted treatments.

Materials and methods: After the development of a general mathematical model on an ideal patient, we have selected 11 advanced stage NSCLC patients who have been monitored through a high sensitive NGS approach on serial blood sampling.

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

Results: Overall, MAF evolution at different clinical evaluation was able to predict either responsiveness or resistance to a given targeted treatment. As expected, no MAF modification have been detected in polymorphic variations (Figure 1).

Discussion: Our data underlined the usefulness of MAF evaluation to monitor clonal evolution in advanced stage NSCLC patients under treatment pressure.

Conclusions and recommendations: Liquid biopsy is an important arrow in the quiver of molecular pathologists and oncologists and should be adopted to monitor tumor clonal evolution under treatment pressure.

Bibliographic references:

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Figure 1. Graphical representation of the evolution of MAF in 11 NSCLC patients monitored by serial blood sampling.