# LIQUID BIOPSY FOR DISEASE MONITORING

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Liquid biopsy is less burdensome than a tissue biopsy and in many advanced NSCLC patients multiple tissue sampling is clinically not feasible. Therefore, plasma is being used more and more for molecular profiling.

The allele frequency of EGFR mutations could be a potential molecular biomarker for the outcome of osimertinib therapy. We assessed the clinical relevance of the allele frequency of *EGFR* mutations in plasma-based circulating tumor DNA (ctDNA) before starting second-line osimertinib treatment in patients with advanced *EGFR* T790M-positive NSCLC. Plasma ctDNA was tested for *EGFR*-activating mutations (*EGFR* deletions in exon 19, L858R, L861Q, S768I) and T790M by means of droplet digital PCR. The allele frequency of *EGFR*-activating mutations in plasma ctDNA before osimertinib initiation was independently associated with progression-free survival and overall survival after adjusting for known clinicopathologic risk factors. A higher T790M allele frequency was associated with a trend towards a shorter PFS and a significantly shorter OS of the patients. Thus, a higher allele frequency of *EGFR* mutations, particularly *EGFR*-activating mutations, in plasma ctDNA is a poor prognostic marker. Further studies on the clinical utility of liquid biopsy are needed.

Somatic copy-number alterations (SCNAs) are associated with drug resistance in patients with advanced *EGFR*-mutated NSCLC treated with EGFR-tyrosine kinase inhibitors (TKIs). We used shallow whole-genome plasma sequencing for genomic profiling of ctDNA in plasma samples from each patient obtained pre-osimertinib and after patients developed resistance to osimertinib. Presence of SCNAs in resistance-related genes in plasma before initiation of osimertinib therapy is associated with a lower response rate to osimertinib and is an independent predictor for shorter survival of the patients. Our approach allows a comprehensive assessment of SCNAs in plasma samples of lung adenocarcinoma patients and has potential to guide genotype-specific therapeutic strategies.