Cell free tumor DNA to monitor response to tyrosine kinase inhibitors in patients with *EGFR*-mutant non-small cell lung cancer

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Background: Monitoring the presence of *EGFR* sensitizing and resistance mutations in *EGFR*-mutant non-small-cell lung cancer (*mEGFR*-NSCLC) patients treated with tyrosine kinase inhibitors (TKIs) may have a clinical impact on the therapeutic strategy.
Methods: *mEGFR*-NSCLC patients treated with first-line TKIs were considered. *EGFR*-sensitive and *EGFR* exon 20 mutations were analyzed in plasma circulating free tumor DNA (cftDNA) collected at baseline, after 8 and 20 days' treatment, and every 4 months of therapy until progression. *EGFR* analyses were performed using PANAmutyper kit (PANAGENE).
Results: Of the 16 *mEGFR*-NSCLC patients treated with first-line TKIs to date, 9 (56%) showed *EGFR*-sensitivity mutation at baseline in cftDNA, 6 had an exon 19 deletion, 1 an exon 21 L861Q mutation and 2 an exon 21 L858R mutation synchronous to exon 20 mutations (these were not identified in tumor tissue). The baseline mutation became undetectable in cftDNA in all *EGFR* exon 19-deleted patients, at different time point from the beginning of TKIs. All these patients had partial response at the first radiological evaluation. The subject harboring *EGFR* L858R mutation synchronous to exon 20 insertion was responsive and showed the disappearance of exon 20 insertion in cftDNA a the first clinical evaluation, whereas *EGFR* L858R disappeared after 4 cycles of treatment. Patient with *EGFR* L858R and T790M didn't respond to TKI.
Conclusion: The disappearance of *EGFR* mutation in cftDNA may be an early parameter of response to TKIs. Moreover, cftDNA may give integrative information with respect to that obtained from tissue analysis, bypassing the problem of tumor heterogeneity.