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The predictive value of circulating tumor DNA dynamics in plasma of EGFR-mutation-positive NSCLC patients on first line tyrosine kinase inhibitors

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Background: The longitudinal analysis of status and level of mutated EGFR gene DNA (mEGFR) in plasma of NSCLC patients (pts) during EGFR-TKI treatment enables the real-time monitoring of the clonal evolution of tumor and detection of resistance mutations. We evaluated the dynamics of mEGFR level in plasma to indicate the acquired resistance to EGFR TKIs and to predict the clinical outcome of NSCLC pts.

Methods: Peripheral blood was prospectively collected from 35 advanced, mEGFR-positive NSCLC pts at the time of diagnosis (baseline) and then every month during the 1st-line EGFR-TKI treatment (erlotinib, gefitinib, afatinib) until clinical progression. The mEGFR ctDNA was analyzed quantitively using cobas EGFR Mutation Test v2 (Roche, Germany).

Results: The median (min-max) PFS was 10 (2-25) months. Significant difference in PFS was found between pts who demonstrated the complete clearance of baseline mEGFR levels in plasma within 1-2 months of treatment (clearers) and pts whose mEGFR levels were similar or higher than baseline (non-clearers): median PFS was 13 months in clearers versus 7 months in non-clearers ($P<0.0036$). PFS was not significantly different between pts with detectable versus undetectable ctDNA at diagnosis and during treatment. In 8 (23%) pts the T790M resistance mutation was detected together with the primary activating EGFR mutation in plasma ctDNA upon progression.

Conclusion: The complete clearance of mEGFR levels in plasma within the first month from the drug administration may predict the long duration of the 1st line EGFR TKI treatment – this observation is to be verified in the larger cohort. The study is ongoing.