In advanced NSCLC around 23% of the tumours harbour EGFR mutations, which are important predictive biomarkers for the efficacy of targeted therapy using EGFR tyrosine kinase inhibitors (TKI) (Fig. 1), and precise determination of the EGFR mutation status is required. Furthermore, emerging mutations during TKI therapy can lead to resistance. The EGFR T790M mutation is the most common acquired resistance mechanism to first- and second-generation EGFR-TKI (Fig. 2).

For a proper selection of patients eligible for TKI therapy, plasma-based EGFR testing analysing cell-free tumour DNA offers a minimally invasive assessment of the EGFR mutation status that can be performed frequently in advanced NSCLC patients.

Several studies demonstrated that OncoBEAM EGFR (RUO) liquid biopsy is an accurate and highly sensitive test for EGFR mutation detection (Fig. 3). OncoBEAM EGFR (RUO) not only reliably detects EGFR mutations in NSCLC patients at baseline before targeted therapy but also at progression (EGFR T790M and C797S acquired resistance mutations) and reveals decreases in mutant EGFR cfDNA levels (activating or T790M) that may be indicative of response to TKI therapy.
OncoBEAM liquid biopsy in advanced NSCLC

Selected publications


Key message: OncoBEAM revealed higher sensitivity than two other technologies by testing cfDNA vs tissue analysis in mCRC and NSCLC samples (extended RAS panel) and enables monitoring of somatic alterations in plasma-derived cfDNA.


Key message: OncoBEAM was applied for cfDNA-based assessment of EGFR mutations in a real-life setting before treatment and during disease progression showing a good correlation with tumour samples and in most cases predicted tumour response and progression before radiologic evaluation.


Key message: OncoBEAM was able to detect inhibition of the drug target, predict response to therapy and detect emergence of drug resistance after therapy with a third-generation EGFR-TKI drug with high concordance to tissue testing (100%, 71% and 84% for EGFR L858R, exon 19 deletion and T790M, respectively).

[4] Oxnard GR et al. (2016): Association Between Plasma Genotyping and Outcomes of Treatment With Osimertinib (AZD9291) in Advanced Non-Small-Cell Lung Cancer, J Clin Oncol 34(28):3375-3382. PMID: 2754477. Key message: OncoBEAM was used in a retrospective analysis in the AURA trial for genotyping of ctDNA as a biomarker for predicting the outcome of a third-generation EGFR-TKI. Patients with T790M in plasma have outcomes with osimertinib comparable to T790M-positive patients by a tissue-based assay. EGFR T790M plasma genotyping had a false-negative rate of 30%, indicating that T790M-negative patients in plasma should undergo tissue biopsy.


Key message: A comparison of EGFR mutation plasma detection platforms demonstrated highest sensitivity for OncoBEAM (Exon 19 del, L858R, T790M) whereas tumour heterogeneity may explain the reduced specificity of T790M mutations.


Key message: Key message: A comparison of EGFR mutation plasma detection platforms demonstrated highest sensitivity for OncoBEAM (Exon 19 del, L858R, T790M) whereas tumour heterogeneity may explain the reduced specificity of T790M mutations.


Key message: OncoBEAM was applied to tumour and plasma samples to retrospectively analyse EGFR mutations, which seem to be a predictive biomarker for the efficacy of sorafenib in patients with advanced NSCLC.


Key message: OncoBEAM was used to assess the impact of the EGFR T790M mutation status in the context of rociletinib treatment demonstrating that T790M clearance could lead to resistance. Furthermore, tumour heterogeneity has important clinical implications since the degree of heterogeneity may be a predictor of rociletinib response, and liquid biopsy can overcome this limitation of tissue biopsy.


Key message: Comparing plasma levels of EGFR-TKI-sensitising mutations with those of the tumour, OncoBEAM showed 87% overall sensitivity and 78% sensitivity for T790M mutations (profiling of 100 EGFR mutation-negative plasma samples yielded no false positives) proving that OncoBEAM represents an alternative for tumour genotyping when an evaluable tumour re-biopsy is not available.


Key message: In plasma from patients with and without EGFR-TKI treatment, the activating and resistant mutations were quantified by OncoBEAM, revealing a peak of the distribution of the mutant allele fraction (MAF) in the 0.1% to 1% range.