Routine Molecular Screening of Patient Samples with Advanced Non-Small Cell Lung Cancer in Circulating Cell-Free DNA Using The Plasma-SeqSensei™ NSCLC RUO Kit at diagnostic in Lyon's hospital.

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Background & objectives

In patients with non-small lung adenocarcinoma cancers (NSCLC), there are 10%–50% of patients exhibit epidermal growth factor receptor (*EGFR*), such as in-frame deletions in Exon 19 (*EGFR* Ex19del) or the *EGFR* p.L858R mutation; and Kirsten rat sarcoma viral oncogene homolog (*KRAS*) sensitizing mutations, such as the *KRAS* p.G12C. The NSCLC treatment has been modified by the availability of *EGFR* and *KRAS* predictive biomarkers. Here, we reported an ultra-sensitive high-throughput targeted DNA sequencing method for circulating free DNA (cfDNA) in terms of high clinical sensitivity detection of targeted somatic alterations. We show the frequency of targeted mutations in circulating cell-free DNA (ccfDNA) at the diagnosis in samples.

Methods

We carried out targeted NGS using the Plasma-SeqSensei™ NSCLC RUO kit on cfDNA on clinical plasma samples. The Plasma-SeqSensei™ NSCLC RUO kit assay covers the *BRAF* alterations in the partial exons 11 and 15, the *EGFR* alterations in the partial exons 18, 19, 20, and 21, the *KRAS* alterations in the partial exons 2, 3, and, and the *PIK3CA* alterations in the partial exons 10 and 21. Identification of the somatic alterations was performed using Sysmex Inostics software (Plasma SeqSensei RUO Software v1.1.3).

Results

We analyzed 136 plasma samples between the 1st of December, 2022, and the 1st of March 2023 at Lyon University Hospital (LHU, France). 99 samples (72.8%) showed no somatic alterations in the limited panel coverage. In the 37 positive samples (27.6%), we found 8.1% *EGFR*, 14.7% *KRAS*, 1.5% *BRAF*, and 2.9% *PIK3CA* mutated samples. Targetable mutations were studied, with a mutant allele frequency (MAF) ranging from 0.11 % to 82.25% in the positive samples and 37.8% of samples are with a MAF inferior to 1%. This mutated repartition found in samples agrees with the caucasian population frequency described in the literature. The time median for releasing the molecular profiling to the oncologists was 7 days.

Conclusion

An effective focal plasma-targeted next-generation sequencing assay (Plasma-SeqSensei™ NSCLC RUO testing kit) for the rapid molecular testing of predictive markers is feasible in routine clinical practice for NSCLC, with a targeted therapy indication.