Liquid biopsies for molecular profiling of mutations in non-small cell lung cancer (NSCLC) patients lacking tissue samples

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BACKGROUND

- Approximately 30% of patients with an adenocarcinoma have a druggable driver mutation.1
- In our experience, 22% of patients are lacking a molecular profile mostly due to insufficient tumor cells in the specimen or poor quality DNA.2
- Cirulating tumor DNA (ctDNA) can be used for detection and quantification of molecular abnormalities as a minimally-invasive tool.
- Moreover, ctDNA analysis may provide a molecular profile when tumor tissue is not available or of poor quality enabling treatment stratification. It can also be used to monitor treatment efficacy and detect resistance mutations.

OBJECTIVES

- To assess the molecular alterations in the ctDNA of NSCLC patients in whom the initial molecular profile or profile at acquired resistance was unknown due to lack of tumor tissue biopsy or insufficient cellularity in the biopsy.
- To assess resistance mutations on treatment.
- To assess the proportion of patients who receive personalized treatment based on these results.

PATIENTS

- We enrolled 116 pre-treated advanced NSCLC patients (1 patient treatment-naïve) with progressive disease described as 2 cohorts:
  - Patients with unknown initial molecular profile
  - Patients with EGFR mutant NSCLC tested in the biopsy.

RESULTS

- From July 2015 to January 2016, 116 patients were enrolled (66% female, 53% never-smoker, 92% diagnosed with an adenocarcinoma subtype, 97% patients (72%) were treated with crizotinib (1 patient treated with Erlotinib). Double EGFR mutation exon 18 and 20 (G719A + S768I) was reported in 1 patients who was treated with crizotinib.

- In the absence of an invasive biopsy, ctDNA can be used as a liquid biopsy for molecular profiling of mutations in NSCLC patients. Liquid biopsy using enhanced Tam-Seq analysis identified cancer mutations in 72% of the study population. Moreover, 22% of the study population subsequently received treatment tailored to the plasma ctDNA detected mutations.

CONCLUSIONS

- We performed a prospective study with all patients (1 patient treatment-naïve) with progressive disease described as 2 cohorts:
  - Patients with unknown molecular profile
  - Patients with EGFR mutant NSCLC tested in the biopsy.

METHODS

- ctDNA of 116 NSCLC patients was analyzed using the Inivata Tam-Seq panel.
- Sequences were generated using Illumina HiSeq 2500 covering regions from 35 cancer-related genes (Figure 1. Inivata Tam-Seq Panel).

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