INTRODUCTION

In non-small-cell lung cancer (NSCLC), overall survival rates are poor as patients are frequently diagnosed at late-stage when treatment options are limited. Circulating tumor DNA (ctDNA) can be used as a non-invasive liquid biopsy for the detection of cancer. However, ctDNA levels have been shown to be low in patients with early-stage disease.

OBJECTIVE

The primary objective of this study was to assess the distribution of ctDNA in baseline plasma samples from early-stage NSCLC patients prior to treatment with curative intent. ctDNA levels were assessed using either patient-specific hybrid capture or amplicon sequencing.

METHODS

100 stage I/II/III treatment-naïve NSCLC patients were recruited to the LUCID (Lung cancer - Circulating tumour DNA) study. The cohort predominantly consisted of stage I/II/III patients (n=460). 55% of patients had adenocarcinoma (Figure A, Figure B).

RESULTS

Patient-specific hybrid capture & INVAR analysis

Exome sequencing identified a median of 328 mutations/patient (IQR: 205–491). 99.8% were private mutations.

Patient and healthy control plasma were analyzed using hybrid capture.

tctDNA was detected in 60/90 (66.7%) patients (mean specificity: 95.63%).

A median of 87,523 informative reads were generated at patient-specific loci (IQR: 44,149–156,446).

For 27 patients, plasma was analyzed using InVisionFirst®-Lung to assess SNSV in genomic regions of 36 cancer-related genes.

tctDNA was detected in 16/27 patients (59%) with a mean 1.67 detections per patient. over, ctDNA was detected down to an allele fraction (AF) of 6 x 10⁻³.

Figure E shows the genes where mutations were identified and the mutation types.

Concordance between ctDNA analysis platforms

Plasma from 17 patients was analyzed using both InVisionFirst®-Lung and INVAR.

Concordance in ctDNA detection was seen in 11/17 patients (64.7%).

Table 1 shows the concordance of ctDNA detection over multiple platforms.

CONCLUSIONS

Overall using both platforms, ctDNA was detected in 66/100 patients at baseline in treatment-naïve NSCLC patients, with detection of ctDNA in 51.7% stage I, 85.7% stage II and 89.5% stage III patients (Figure G, Figure H).

Analyzing different historical subtypes, overall ctDNA was detected in 79% of squamous cell carcinomas and 60% of adenocarcinomas (Figure G).

Overall ctDNA results

- Tumor volumetric data was available for 43 patients where ctDNA was analyzed.
- Figure I shows a significant correlation between ctDNA fraction and tumor volume in patients with stage I cancer disease (Pearson’s r = 0.52, p = 3 x 10⁻⁴) where ctDNA was detected.