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INTRODUCTION



Two major approaches have emerged for detecting ctDNA in cancer patients: tumor-informed and tumor agnostic approaches.



Tumor-informed approaches utilize the patient's tumor to create a custom panel specific for detecting ctDNA based on variants found in the tumor. Tumor agnostic approaches use a fixed panel assay design for all patients, and while convenient, are generally less sensitive compared to tumor-informed assays.



A personalized, tumor-informed (TI) ctDNA analysis offers the potential to detect minimal residual disease (MRD), early recurrence or monitor tumor response in patients diagnosed with non-small cell lung cancer (NSCLC).



This study aims to evaluate the comparative effectiveness of TI ctDNA monitoring in NSCLC and explore its potential to complement or replace imaging.



METHODS

We did a study using NeXT Personal®, an ultra-sensitive, tumor-informed ctDNA assay that uses whole genome sequencing (WGS) of tumor and matched normal samples combined with advanced analytics to accurately identify up to ~1,800 somatic variants (SVs) specific to the patient's tumor, which enables enhanced sensitivity compared to other tumor-informed panel approaches that typically rely on up to ~50 whole exome sequencing (WES) based variants. A personalized panel is created, targeting these variants and then used to sequence cell-free DNA extracted from patient plasma samples for ultra-sensitive detection of ctDNA.



METHODS

Surveillance results were considered concordant if there was evidence of disease progression (PD) or recurrence on imaging tests corresponding to a positive or increased ctDNA in plasma, while stable disease (SD), responses (CR, PR) or no evidence of disease aligned with a decrease or negative ctDNA result. Statistical association was evaluated using Fisher's exact test. Patient demographics, tumor characteristics, and genomic analysis were recorded.



RESULTS



We have data in 112 lung cancer patients that underwent testing. In 84% we had sufficient tumor tissue to run the ctDNA assay.



Most of the patients were female (57%), with a median age of 72 years, Non-Hispanic White (NHW) patients were 79%, former or never smokers 96%.



Overall, there was a 46% positive detection rate, of which 45% were in the ultrasensitive range (<100 PPM) and 26% below 10 PPM.



There was a 93% concordance between ctDNA and CT scan responses ($p < 0.001$).



Among patients with metastatic disease that had radiological response (ORR: CR/PR) 93% had undetectable ctDNA, among patients that have SD/PD 92% had detectable ctDNA.



The sensitivity was 100% (CI:95% from 73% to 100%) and specificity 73% (CI:95% from 61% to 83%) $p < 0.000001$.



We plan to do a longer follow up of this cohort to assess progression free survival and overall survival based on ctDNA.



CONCLUSIONS



A Personalized, tumor-informed ctDNA assay was able to accurately correlate with radiologic imaging in most of the NSCLC patients, particularly outside the CNS. The presence or absence of ctDNA was also predictive of response.



We showed that ctDNA not only can be used to assess MRD after surgery but also monitor tumor response in metastatic disease.



There are challenges in making the test based on tissue availability that need to be considered.



More and larger studies are needed to validate these results and follow up to evaluate overall survival.



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