Establishing an academic hospital based liquid biopsy platform for mrd testing in breast cancer patients

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Abstract

Background: The detection of minimal residual disease (MRD) requires the capacity to capture very minute amounts of circulating tumor DNA in the blood. Tumor informed assays have demonstrated the highest sensitivity for MRD detection. Although commercially available assays for MRD are now available, our objective is to develop a hospital based liquid biopsy platform to reduce costs.

Methods:

Our pipeline begins standardized tumor and plasma collection and processing, followed by the clinical grade sequencing of a FFPE tumor and germline sample. A report with somatic mutations is generated within 2 weeks and used to identify 5-6 variants per patient that are used for the development of digital droplet PCR assays. ctDNA tests are first validated with the patient tumor's DNA and then used for MRD detection in the patient's plasma.

Results: The analytical performance of our assays demonstrate high sensitivity (up to 97% for Variant Allele Frequency ≥0.1%), and high specificity (99%) across a concentration range (0.005% to 5%). This platform has been used for the analysis of over 500 plasma samples from 118 patients participating in the Q-CROC-03 and TRICIA clinical trials. These studies have confirmed the prognostic value of ctDNA detection in high risk triple negative breast cancer patients (TNBC). Patients with ctDNA negative plasma at the end of neoadjuvant chemotherapy and prior to surgery had a significantly higher relapse free survival than patients with ctDNA positive results (p = <0.0001, Hazard Ratio (HR) = 0.052(95%CI = 0.025 – 0.12). We were able to detect MRD after surgery in 24 out of 26 (92% sensitivity) patients who relapsed with a lead time of 12 months prior to clinical relapse. ctDNA tests can be generated on average in 21 days after tumor sequencing data is obtained, thus enabling the delivery of MRD results in a timely manner for clinical decisions in the adjuvant breast cancer setting.

Conclusion:

Our hospital based tumor informed ctDNA assays have identified a very good prognostic group in high risk TNBC patients and offer the opportunity to perform real time MRD monitoring at a reduced cost in an academic hospital setting.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.