Experiences gained from real-world clinical testing of cancer patient plasma, using a highly sensitive, personalized circulating tumor dna assay

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Abstract

Background

Circulating tumor DNA (ctDNA) represents a promising tool for detection of minimal residual disease and treatment monitoring in patients with cancer. Highly sensitive assays that detect minute quantities of ctDNA are required. Despite its promise, there is much to be learned about the utility and technical performance of ctDNA assays, and sample characteristics in the clinical setting across cancer types that may have differing shedding rates depending on their underlying biology.

Objective

Leverage pan-cancer data from a large cohort of patients, tested with the tumor-informed RaDaR assay, to describe ctDNA metrics from real-world samples.

Methods

We analyzed data from 395 patients (n=1122 samples). Tumors included breast (n=216; 89 HR+/HER2-, 22 HER2+, 17 TNBC, 88 unknown), colorectal (CRC, n=73), pancreatic (n=28), lung (n=18), head and neck (H&N, n=18), and other malignancies (n=42). Sampling wasn't limited to any particular timepoint during treatment. To explore ctDNA quantities in different settings, ctDNA+ samples were stratified by estimated variant allele frequency (eVAF) ≥0.01%, and <0.01%.

Results

ctDNA was detected in 23.8% (267/1122) of samples. Amongst ctDNA+ samples, eVAF ranged from 0.0002% to 24.8%, and 31.1% had eVAF <0.01%. Considering individual cancer types, 22%, 33.3%, 70.8%, 31.5% and 12.5% of positive samples in breast, CRC, pancreatic, lung and H&N had eVAF <0.01%. The enrichment for ctDNA+ samples with low eVAF in pancreatic cancer may indicate this as a 'low shedder' malignancy. Across all tumor types, considering samples where staging information was available, 100%, 39%, 22% and 28% of ctDNA+ samples from patients with stage I, II, III and IV disease respectively, had eVAF <0.01%. Of 27 ctDNA+ plasma samples from patients with HR+/HER2- breast cancer, 30% had eVAF <0.01%.

Conclusion

Our data highlight the range of ctDNA levels encountered across cancers of different anatomical location, subtype, and stage, when performing real-world clinical testing of cancer patients. In particular, a significant portion of ctDNA+ samples had low levels of ctDNA, with a marked occurrence in the pancreatic cohort. These findings highlight the importance of sensitivity to reduce the risk of false negative results amongst samples with low eVAF. Additional technical and clinical observations will be presented.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

All authors are employees of NeoGenomics, Inc