Analytical validation of a robust integrated genomic and epigenomic liquid biopsy for biomarker discovery, therapy selection, and response monitoring

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Introduction

Despite its revolutionary impact, cancer genome alone provides little information on tumor phenotype or functional state, which are governed by epigenetic mechanisms, notably methylation of regulatory regions. Tumor and host epigenetic methylation signatures reflect not only tumor phenotype, such as histology, prognosis, protein expression, and functional sub-type, but also that of the tumor microenvironment and the patient, including immune status, therapy-related adverse events, comorbidities, and disease location. Epigenetic markers also provide more sensitive and precise measures of tumor burden, opening up applications for longitudinal therapy response and monitoring. Here we report the initial validation of GuardantINFINITY, a liquid biopsy assay combining genomic information from >900 genes with characterization of the blood-quiet regulatory methylation, both at single-molecule sensitivity from a single tube of peripheral blood.

Methods

Analytical performance of GuardantINFINITY was a Research Use Only (RUD) setting was assessed following non-US/SCC Working Group Guidelines using 914 samples which consisted of pre-characterized cancer cell lines, healthy-normal donor-derived cfDNA, and cancer patient cfDNA samples. The panels were tested at both 5ng and 30ng cfDNA input levels, and all samples passed sequencing QC metrics prior to analysis. The cancer samples were titrated at both 5ng and 30ng cfDNA input levels, and all samples passed sequencing QC metrics prior to analysis.

Results

Analytical accuracy of GuardantINFINITY was assayed in the full panel, using cell-line material and assessed in the full panel. The inset figure shows that this strong correlation holds down to the lowest observed MAF and CN values. Of the two panels. The inset figure shows that this strong correlation holds down to the lowest observed MAF and CN values.

Conclusion

GuardantINFINITY™ is a patient-care ready liquid biopsy capable of integrating genomic and epigenomic analysis of all solid tumors at single-molecule sensitivity. In addition to traditional genotyping compatible with Guardant360 for more information, visit www.guardanthealth.com