Analysis of the Presence of TP53 Mutations in Targeted NGS Profiles of EGFR wild-type, NSCLC patients with Poor Prognosis

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Background and Methods

Blood-based molecular tests can help target treatments for Non-Small Cell Lung Cancer patients. The GeneStrat® blood-based mutation test provides actionable mutation information in 72 hours to aid in rapid treatment decisions. The GeneStrat® serum protein test measures acute phase reactant proteins in the blood known to be associated with aggressive cancers, providing predictive and prognostic information by classifying patients as VeriStrat® GOOD® (VS-G), Poor (VS-P). Patients with a VS-G classification should be referred to an oncologist for clinical outcomes relative to those with a VS-P status. GeneStrat® is also predictive of response to EGFR-TKI therapies. GeneStrat® testing may be conducted as a reflex test for patients found to be EGFR wild-type (WT) through the Biodesix Lung Reflex® testing process. Treatment options for patients with NSCLC who are EGFR WT and VS-P are limited, thus the addition of extensive genomic and proteomic testing may provide more comprehensive clinical information to support treatment planning and patient placement in clinical trials. For this study, we profiled circulating free DNA (cDNA) in matched plasma specimens determined to be EGFR WT (by droplet digital PCR) and VS-P (n=11) with a targeted next-generation sequencing (NGS) test for actionable somatic variants in 15 genes. Six of the 11 plasma samples contained TP53 mutations, which included missense, splice-site, and frameshift. These patients are in development of TP53-based therapies. These include pre-clinical and clinical trials for agents such as APR-246 (a PRIMA-1 analogue), a compound that targets re-activation of TP53. Targeted profiling using NGS on cDNA from plasma can identify actionable mutations in patient samples with a poor prognosis as determined by the VeriStrat® test. It is likely that other targets associated with current therapies may be identified with additional profiling. Expanded profiling of EGFR WT/VS-P patients using NGS tests that measure additional somatic variants, indels, rearrangements, and amplifications is underway. We expect that these studies will demonstrate the utility of NGS profiling to identify additional treatment options for VS-P patients with NSCLC.

Results

Table 1: System Performance Qualification using Analytic Controls. Pre-Qualified Standards were purchased from Horizons Discovery and evaluated by NGS profiling at Biosides (R > 0.978).

Table 2: VeriStrat® Reflex to Broad Molecular Profiling by GeneStrat® NGS. EGFR WT/VS-P samples were analyzed using a commercially available 15 gene NGS panel.

Table 3: Sequencing Metrics of VS-P Samples and Controls Using NGS Panel.

Conclusions

- 56% (6/11) of VS-P had a potential target of therapy identified by broad molecular profiling.
- Targeted profiling using NGS on cDNA from plasma can identify actionable mutations in patient samples with a poor prognosis as determined by the VeriStrat® test. It is likely that other targets associated with current or developing therapies may be uncovered with additional profiling.
- Similar, but expanded profiling of EGFR wild-type/VS-P patients that measures additional somatic variants, indels, and amplifications is underway.

References


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