Utility of blood-based genomic and proteomic tests for Non-Small Cell Lung Cancer

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Abstract
Background: Despite advances in treatment for lung cancer, the disease remains challenging to manage. While cure through surgery is a desired goal, most patients present at an advanced stage, requiring biomarker-guided therapy. However, recent studies have found the median turn-around time for tissue-based mutation results was 12 days (range 1-54) for newly diagnosed patients and 27 days (range 1-146) for patients with acquired T790M resistance. Tissue availability and results turnaround time can delay the optimal treatment of patients with NSCLC.

Methods: To address this challenge, we have developed the Biodies Lung Reflex™ test, which includes the GeneStrat™ (Digital Droplet™ PCR) and VeriStrat™ (MALDI-ToF mass spectrometry) tests. Both technologies are innovations in clinical laboratory diagnostics. GeneStrat testing delivers variant specific results for EGFR, KRAS, BRAF, ALK, RET and ROS1, while VeriStrat proteomic profiling classifies patients who are EGFR mutation negative by expected outcome, assigning a VeriStrat status of Good, Intermediate or Poor. These non-invasive blood-based tests reduce result turnaround time to 3 days, and are rapid, reliable and accurate.

Results: Here we report on factors critical to demonstrating the validation and utility of the GeneStrat and VeriStrat tests and review on market performance metrics for each. To enhance the utility of the Biodies Lung Reflex strategy even further, we also introduce data supporting the PD-L1 test concept currently in development.

Conclusions: Blood-based tests for the rapid, reproducible and sensitive detection of both nucleic acid variants and serum proteomic profiles are highly suited for diagnostics.

Background and Methods

Figure 1. Biodies Lung Reflex Strategy. The schematic highlights Biodies’ approach to the continuum of care for patients previously diagnosed with lung cancer. Tests currently performed in the Biodies CLIA Laboratory are in the purple and green shading.

Figure 2. Overview of Processing Steps in the Biodies Lung Reflex Test Strategy. The testing process is initiated when whole blood drawn into blood collection tubes (for GeneStrat testing) or dried serum spot cards (for VeriStrat testing) arrive at the Biodies Laboratory and all necessary documentation is confirmed. Patient samples are accessioned and processed through parallel workflows to isolate circulating DNA and RNA, or to recover serum proteins. For ddPCR analysis, samples are processed using the Bio-Rad Xpress 200 ddPCR system and droplet counts are evaluated using QuantaSoft. For MALDI-ToF analysis, samples are processed on an Ab SciFlex SI-MS and spectra are analyzed using the VeriStrat algorithm. Test Result Reports are generated from the parallel analyses.

Figure 3. GeneStrat Validation Studies. A. Droplet distributions from positive samples for each variant. B. Clinical validation: DNA tests (n=151 total samples) and EML4-ALK RNA test (n=24).

Figure 4. GeneStrat Mutation Detection Rates. The percentage of GeneStrat DNA/RNA variant tests that yielded a Positive or a Negative result over a contiguous three month period. Note: The GeneStrat RET and ROS17 tests launched February 1st 2017 and are not represented in this figure.

Figure 5. VeriStrat Clinical Validation. A. Spectra representing a VeriStrat Good and Poor result. B. Kaplan-Meier (KM) curves of overall survival (OS) by VeriStrat classification. (left KM) an observational study for systems-therapy naive patients administered platinum-based chemotherapy, and (left KM) the PRINCE prospective study for previously treated patients receiving either single agent chemotherapy or erlotinib. C. Patient outcomes from multiple studies by VeriStrat classification.

Figure 6. VeriStrat Classification Rates. The percentage of VeriStrat tests that yielded either a Good, Poor or Indeterminate result over a 12 month period.

Figure 7. Biodies Lung Reflex Test Turn Around Time over a 12 month period. Data exclude weekends/holidays and samples held for >24 hours due to lack of sufficient blood available for testing.

Conclusions

Blood-Based Biodies Lung Reflex testing for the rapid, reproducible and sensitive detection of both nucleic acid variants and serum proteomic profiles are highly suited for diagnostics.

Over 94% of GeneStrat™ and VeriStrat™ results were generated within 72 hours of sample receipt.

The GeneStrat test is highly sensitive and measures actionable mutations that can direct the use of targeted therapy, without the need for tissue biopsy.

• Positive variants ranged from 1.2% - 15.8% with greater than 4,000 individual cases evaluated

• For EGFR wild type or unknown patients, VeriStrat test classified 78% as Good, 20% as Poor and 2% as Indeterminate with close to 4,000 individual cases evaluated.

• While patients with a Good result may benefit from systemic therapy, those with a Poor result may derive little clinical benefit from platinum-based therapies or EGFR TKIs

• Biodies Lung Reflex test provides valuable clinical information to optimize treatments for patients with NSCLC by identifying patients likely to benefit from targeted agents and supporting patient physician conversations regarding prognosis and treatment decisions.

• The VeriStrat test may identify a subsets of patients who are candidates for molecular profiling to inform alternative therapies and clinical trial enrollment options.

• Development of future tests to help with immunotherapy treatment decisions is ongoing.

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