Summary

Standard tumor biopsy mutation testing for patients with non-small cell lung cancer (NSCLC) is often limited by sample availability and can increase patient risk due to complications. GeneStrat™ mutation testing uses a low risk blood draw to provide accurate results and offers a 72 hour turnaround time, supporting critical treatment decisions. This study will report on the performance of GeneStrat, a blood-based CLIA-certified Laboratory Developed Test (LDT). The test workflow is comprised of three components: (i) a whole-blood collection kit that ships at ambient temperature; (ii) circulating nucleic acids are isolated from plasma for analysis using Droplet Digital™ PCR (ddPCR), and (iii) a secure laboratory information management system (LIMS) for sample accessioning and test result generation. Metrics associated with the circulating tumor DNA (ctDNA) that detects EGFR, KRAS, and BRAF mutations for patients with advanced stages of cancer will be presented. Specifically, ddPCR testing covers the EGFR (exons 19, 21), BRAF (exons 11, 15), and KRAS (exons 2, 3, 4) mutation hotspots.

Background and Methods

- Twenty-nine (31%) samples included in this data set were analyzed with 5376 individual variant targets. The majority (~90%) of samples were aligned with a lung cancer diagnosis. The percentage of tests for which we have detected mutations are 10.7% for EGFR, 15.4% for KRAS, 12.5% for KRAS and 1.2% for BRAF. In addition, the ddPCR testing of the somatic gene variants listed above, we report on a newly launched GeneStrat gene fusion assay that detects EML4-ALK variants in circulating tumor RNA (ctRNA) isolated from blood (invivo). The percentage of tests for which we have detected EML4-ALK fusion variants is 6%. In summary, we have developed highly sensitive and clinically-actionable blood-based assays as part of the GeneStrat test with clinical sensitivity for available mutations ranging from 85-96% and concordance ranging from 92-99%. Clinical specificity for all mutations evaluated was 100%. GeneStrat expands the available testing options and supports earlier treatment decisions for patients newly diagnosed with lung cancer or in the absence of a tissue biopsy.

Results

A.

Available Mutations

<table>
<thead>
<tr>
<th>Mutations</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>100%</td>
<td>95.8%</td>
<td>98.4%</td>
</tr>
<tr>
<td>KRAS</td>
<td>95.8%</td>
<td>100%</td>
<td>98.4%</td>
</tr>
<tr>
<td>EML4-ALK</td>
<td>100%</td>
<td>96.4%</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

B.

Turn Around Time (%)

- 96.4% of the DNA samples were tested within 24 hours.
- 94.9% of the DNA samples were tested within 48 hours.
- 92% of the DNA samples were tested within 72 hours.
- 86.7% of the DNA samples were tested within 4 days.
- 79.2% of the DNA samples were tested within 7 days.
- 75.0% of the DNA samples were tested within 14 days.
- 72% of the DNA samples were tested within 28 days.

C.

The prevalence of EML4-ALK variants in lung cancer patients is 6%.

Conclusions

- 94% of the GeneStrat DNA test results were generated within 72 hours of sample receipt.
- 94% of DNA tests were ordered by physicians treating lung cancer patients.
- Detected results for individual variants ranged from 12.5% - 15.8%.
- 75% of EGFR T790M or T790M only variants were detected.
- 65% of the EML4-ALK variant tests were detected.

In conclusion, GeneStrat is a targeted liquid biopsy mutation test with a best in class turnaround time. The test identifies actionable mutations with proven clinical utility for diagnosis or therapy monitoring.

Acknowledgments

We would like to thank all members of the Biodesix team.

References

8. Boston, MA.

Upcoming Bio-Rad Sponsored Talk

March 10–11, Hilton San Francisco Union Square

3:00 PM - 5:00 PM

Symposia 2, Hilton San Francisco Union Square