Clinical outcomes in patients with advanced NSCLC treated with targeted therapies, with actionable mutations identified by InVisionFirst ctDNA assay

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INTRODUCTION

• Circulating tumor DNA (ctDNA) can be used for somatic mutation detection, such as EGFR, BRAF or KRAS mutations as well as fusions (ALK and ROS1), in NSCLC patients.
• ctDNA-based comprehensive germline profiling (CGP) using multigene next-generation sequencing (NGS) panels is rapidly gaining traction in clinical practice.
• However, prospective clinical outcomes of patients with genomic alterations in plasma ctDNA by NGS panels remain poorly described.
• Here, we describe outcomes in advanced NSCLC patients with actionable alterations identified in plasma by InVisionFirst™-Lung.

METHODS

• We performed a pooled-analysis across advanced NSCLC patients with actionable alterations detected by amplicon-based NGS (InVisionFirst-Lung).
• Patients treated with matched targeted therapies evaluable for disease control at 3 months were collated for clinical outcomes analysis, based on disease stage and class of therapy.
• All patients provided written consent approved by the institutional ethics committee under which the studies were conducted.

RESULTS

• 82 patients were evaluable for outcome analyses.
• 71 patients (87%) had disease control at 3 months of therapy.
• The response rate at 3 months was 61%.

### Table 1. Summary of patients with actionable genomics alterations detected by in vivo ctDNA testing in these studies. Patients included those with all the classes of alterations predicting response to current FDA approved drugs (EGFR activating mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene fusions and BRAF mutations).

<table>
<thead>
<tr>
<th>Genomic alteration</th>
<th>Number of patients</th>
<th>Response at 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK gene fusions</td>
<td>18</td>
<td>100%</td>
</tr>
<tr>
<td>BRAF mutations</td>
<td>17</td>
<td>60%</td>
</tr>
<tr>
<td>EGFR activating mutations</td>
<td>39</td>
<td>83%</td>
</tr>
<tr>
<td>EGFR T790M mutations</td>
<td>23</td>
<td>57%</td>
</tr>
<tr>
<td>ROS1 gene fusions</td>
<td>31</td>
<td>88%</td>
</tr>
<tr>
<td>ROS1 gene fusions and BRAF mutations</td>
<td>32</td>
<td>73%</td>
</tr>
</tbody>
</table>

### Figure 2A & B (Case studies of 2 patients A) EML4-ALK fusion patient previously untreated with TKI, who clinically progressed on crizotinib at 22 months and B) EML4-ALK fusion patient previously untreated with targeted therapy, with durable clinical response to ceritinib at 6 months follow-up.

CONCLUSION

• Clinical outcomes in patients who have been treated with targeted therapy based on actionable alterations detected by amplicon-based NGS ctDNA analysis by InVisionFirst are consistent with those reported based on tissue profiling.
• ctDNA molecular profiling using InVisionFirst is an accurate and reliable tool for the detection of clinically relevant molecular alterations in advanced NSCLC patients.

ACKNOWLEDGEMENTS

• Clinical patients and their families
• The staff and investigators at each study site: clinicians, study coordinators and biobank staff

REFERENCES:

3. NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer
5. Rosell et al NEJM

Figure 2: Kaplan-Meier curve of time to progression/termination of therapy (with 95% CI) of the combined analysis of the Untreated, Untreated with Targeted Therapy, and the Recurrent patients.

Figure 3: Kaplan-Meier curve with stratification of groups, demonstrating the progression-free survival (PFS) for patients on an appropriate targeted therapeutic agent as determined by the identification of an actionable mutation. There was no significant difference in PFS between these groups (p=0.615) as described previously.

Figure 1. The InVisionFirst™-Lung assay identifies SNVs, Indels, CNVs and gene fusions with whole gene and gene fusions, using an amplicon-based technology, in selectively amplify genomic breakpoints. The sequence of the junctions are then identified using NGS, allowing the genomic breakpoint in ctDNA to be mapped.

Figure 2: Kaplan-Meier curve of time to progression/termination of therapy (with 95% CI) of the combined analysis of the Untreated, Untreated with Targeted Therapy, and the Recurrent patients.