INTRODUCTION

Liquid biopsy has been increasingly used in cancer diagnosis, monitoring of therapy response and minimal residual disease (MRD). In this study, we report the development of a novel PredicineALERT liquid biopsy solution for personalized and generalized MRD detection, regardless of tumor tissue status.

If baseline sample (tissue or liquid biopsy such as blood, urine, CSF) is available, a personalized PredicineALERT MRD approach is recommended where the PredicineWES assay will be used for genome-wide coverage of coding regions and the 600-gene PredicineATLAS™ NGS panel for in-depth molecular profiling. Variants detected in baseline samples will be used for personalized MRD detection with assay sensitivity down to 0.005%.

If baseline sample is not available, generalized MRD approach will leverage the multidimensional genomics and epigenomic variants in liquid biopsy.

Important cancer-related actionable genes are included in the PredicineALERT MRD platform to provide actionable insights for MRD-positive patients.

METHODS

PredicineWES:

- Somatic mutations, Indels
- Copy number gain and loss
- Gene fusion
- Pathogenic germline variants
- Tumor fraction, TMB, MSI, HRD

PredicineWES assay features:

- Incorporating 20,000-gene WES panel and 600-gene PredicineATLAS panel
- Deep sequencing (20,000x, 0.25% LOD) on 600-cancer genes and important DNA fusions
- Whole exome coverage at 2,500x (1% LOD) enables genomics profiling beyond cancer genes
- Exome-wide SNP skeleton enhances LOH and CNV detection
- Precise estimation of tumor fraction, HRD score, tumor mutation burden (TMB) and microsatellite instability (MSI)
- Applies to tissue and liquid biopsy samples, including plasma and urine

RESULTS

PredicineALERT MRD assay:

Fig. 2: Workflow for PredicineALERT MRD assay, regardless of baseline sample availability

PredicineWES: Table 1: PredicineWES detects more variants than PredicineCARE panel in plasma

<table>
<thead>
<tr>
<th></th>
<th>PredicineWES</th>
<th>PredicineCARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic</td>
<td>284</td>
<td>103</td>
</tr>
<tr>
<td>Somatic</td>
<td>80</td>
<td>23</td>
</tr>
<tr>
<td>Somatic</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Somatic</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>Somatic</td>
<td>85</td>
<td>4</td>
</tr>
<tr>
<td>Somatic</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>Somatic</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

PredicineWES detects and confirms all copy number variations (CNV) detected in patient plasma samples using the 152-gene PredicineCARE CLIA-certified NGS assay

PredicineALERT - Case study of baseline informed, personalized MRD assay:

- mCRC plasma samples profiled by PredicineWES, somatic mutations are selected to design PredicineALERT personalized MRD panel.
- Patient plasma cfDNA is diluted in normal cfDNA background at five titration levels: 0.1, 0.05, 0.025, 0.01 and 0.005%.

Fig. 4: Personalized MRD detection in plasma samples

A. CF distribution of PredicineWES-based mutations selected for personalized MRD monitoring
B. MRD assay specificity study

CONCLUSIONS

We have developed a proprietary PredicineALERT MRD liquid biopsy assay that can detect cancer variants down to 0.005% with actionable variants detected simultaneously. PredicineWES assay is used to generate genome-wide and in-depth baseline profiling, enabling personalized and ultra-sensitive monitoring of therapy response and disease recurrence.