Tissue Sequencing Metrics

<table>
<thead>
<tr>
<th>Gene or Pathway</th>
<th>All Tissue</th>
<th>DNA Repair-related Alterations</th>
<th>Alteration Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>8.6%</td>
<td>8.6%</td>
<td>100%</td>
</tr>
<tr>
<td>BRCA1</td>
<td>7.7%</td>
<td>7.7%</td>
<td>91%</td>
</tr>
<tr>
<td>BRCA2</td>
<td>5.9%</td>
<td>5.9%</td>
<td>92%</td>
</tr>
<tr>
<td>CHK1</td>
<td>13.6%</td>
<td>13.6%</td>
<td>86%</td>
</tr>
<tr>
<td>DDR2</td>
<td>5.7%</td>
<td>5.7%</td>
<td>84%</td>
</tr>
<tr>
<td>FANCA</td>
<td>3.4%</td>
<td>3.4%</td>
<td>67%</td>
</tr>
<tr>
<td>PALB2</td>
<td>1%</td>
<td>1%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Tissue and Plasma Concordance

- The plasma assay detected more alterations than the tissue assay in 4% of patients. The tissue test detected more alterations than the plasma test in 2% of patients.
- There was high concordance between the alterations detected in tissue and plasma samples.
- The plasma assay detected the same BRCA2/CDK12 alteration in tissue for 86% and 71% of patients, respectively.

Plasma Sample Overview

- Plasma samples were sequenced using a cell-free DNA-FMI assay to identify deleterious germline or somatic alterations in BRCA1, BRCA2, ATM, or other DNA repair (DRR) genes.
- PALB2, RAD51D, RAD14B, RAD121, RAD121D, and RAD124D.
- The plasma assay detected deleterious missense mutations, protein truncations, and alterations in a deleterious DDR gene.
- The plasma assay detected alterations in tissue for 86% and 71% of patients, respectively.

Plasma and Tissue DDR Gene Alterations

- The BRCA2/CDK12 alteration frequency was 12.6% in tissue compared to 10.2% in tumor tissue.
- The plasma assay detected more alterations in BRCA2/ATM than the tissue assay.
- Most of the tissue samples were archival and may be less representative of the representative of the metastatic disease state.

References

1. Frampton et al. J Mol Diagn 2017;1:1
2. The TRITON2 study is enrolling mCRPC patients with a deleterious DDR gene alteration to evaluate the potential benefit of treatment with the PARP inhibitor rubraca.
3. Tissue and plasma assays were both used to successfully identify patients with a DDR gene alteration.
4. Alterations were frequently observed in several cancer related pathways, including DDR, PI3K/AKT, MAPK, and Wnt.
5. The tissue vs plasma discordance was between the alterations detected with the tissue and plasma assays.
6. The plasma assay detected the same BRCA2/CDK12 alteration in tissue for 86% and 71% of patients, respectively.

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