Whole-genome cell-free DNA (cfDNA) changes as a dynamic blood-based biomarker for early response assessment of advanced tumors

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Objectives

- The assay had consistent predictive performance in patients on immunotherapy as well as breast and lung cancer subsets.
- The confirmed predictions of progression were based on blood samples taken a median of 5.5 weeks before imaging and clinical evaluation.

Longitudinal Cohort

Patients treated for advanced cancer face considerable uncertainty in real time regarding the effectiveness of systemic therapies while incurring a serious burden of cumulative toxicity and out-of-pocket expenses. Today, imaging (CT, PET, MRI), the standard for response assessment, typically requires 3-4 months or longer on therapy before confident conclusions can be made.

Methods

We performed whole-genome analysis of cfDNA from serial blood samples in 69 prospectively enrolled patients receiving treatment for advanced cancer.

- Increases in tumor-derived cfDNA were strongly predictive of disease progression at first follow-up and shorter progression-free survival.
- The assay had consistent predictive performance in patients on immunotherapy as well as breast and lung cancer subsets.

- The confirmed predictions of progression were based on blood samples taken a median of 5.5 weeks before imaging and clinical evaluation.

Results

The change in cancer-associated signal after the start of treatment has previously been shown to correlate with progression. We quantified the change in DNA sequence using deep sequencing of pooled cfDNA at multiple time points during treatment for 42 advanced tumor patients (n=25). Footnoted cases showed clear clinical progression.

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Conclusions

- Analyzing cfDNA early in the course of a new therapy holds promise to identify patients with disease progression faster than traditional methods.
- This technology may enable early switching to other potentially effective therapies, increasing the value proposition of all delivered treatment.
- Predictive value of this approach appears to be independent of the underlying tumor type and therapeutic modality, which could facilitate broad clinical application.

- Further studies are ongoing to develop this assay for use in clinical practice.

Acknowledgements & References

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Table 1. Patient characteristics; 2017-2018.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Race</th>
<th>Type</th>
<th>Stage</th>
<th>Line of therapy</th>
<th>Type of treatment</th>
<th>Outcome</th>
<th>cfDNA (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-75</td>
<td>F</td>
<td>White</td>
<td>Breast</td>
<td>II</td>
<td>1st</td>
<td>Immunotherapy</td>
<td>Progression</td>
<td>12.3 (5.9)</td>
</tr>
<tr>
<td>76-80</td>
<td>M</td>
<td>Black</td>
<td>Lung</td>
<td>IIIB</td>
<td>0.5</td>
<td>Chemotherapy</td>
<td>Non-progression</td>
<td>3.1 (1.8)</td>
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<tr>
<td>81-85</td>
<td>F</td>
<td>White</td>
<td>Breast</td>
<td>IIIB</td>
<td>2.0</td>
<td>Radiation Therapy</td>
<td>Progression</td>
<td>2.5 (1.3)</td>
</tr>
</tbody>
</table>

References

1. Adalsteinsson, VA, et al., "Scalable whole-exome sequencing of cell-free DNA reveals high concordance with metastatic tumors".