Circulating Tumor DNA for Early Risk Stratification of Oligometastatic Lung Cancer

Presented by:
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Disclosure & Study Team

• Disclosure: A.A.C. has patent filings related to cancer biomarkers, and has licensed technology to Droplet Biosciences, Tempus Labs, LiquidCell Dx, and Biocognitive Labs. A.A.C. has served as a consultant/advisor to Roche, Tempus, Geneoscopy, Illumina, Myriad Genetics, Invitae, Daiichi Sankyo, AstraZeneca, AlphaSights, DeciBio, and Guidepoint. A.A.C. has received honoraria from Agilent, Roche, and Dava Oncology. A.A.C. has stock options in Geneoscopy, research support from Roche, Illumina and Tempus, and ownership interests in Droplet Biosciences and LiquidCell Dx.

• This study was supported by funding from Tempus Biolabs, the V Foundation, the Alvin J. Siteman Cancer Research Fund, and the National Cancer Institute.

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Background

• Oligometastatic lung cancer can be treated with consolidative radiotherapy, but it is challenging to know which patients will benefit from radiotherapy and which will not

• Imaging may not represent a patient’s true burden of disease, because there may be micrometastatic disease beyond the limited number of lesions seen on the scan

• Can we use liquid biopsy to improve precision & clarity in this space, and enhance radiotherapy decision-making?
The conundrum of oligometastatic disease management.
Methods

• We performed a real-world study of 309 patients with oligometastatic non-small cell lung cancer (NSCLC) treated at both academic and community practices nation-wide

• All 309 patients had a confirmed diagnosis of metastatic NSCLC, and had liquid biopsy ctDNA analysis performed prior to radiotherapy

• ctDNA analysis was with the Tempus xF assay, with mutations identified using VarDict and pathogenic or likely pathogenic mutations determined by SnpEff

  • Only pathogenic or likely pathogenic mutations were considered for ctDNA detection and quantitation
Question: Can ctDNA detection before XRT stratify survival outcomes in oligometastatic NSCLC patients? If so, ctDNA could represent a precision biomarker to determine which oligometastatic patients should be prioritized for consolidation XRT.
Results: ctDNA detection pre-RT predicts PFS

\[ P = 0.004 \]
\[ HR = 1.57 \]

\( n = 309 \) patients
Results: ctDNA detection pre-RT predicts OS

\[ P = 0.030 \]
\[ HR = 1.65 \]

\( n = 309 \) patients
Results: ctDNA levels pre-RT predict PFS

$P = 0.008$

$n = 309$ patients
Results: ctDNA levels pre-RT predict OS

$P = 0.007$

$n = 309$ patients

No. at risk

- Not Detected: 78, 48, 21, 10, 6, 2, 0
- Max VAF <0.1: 167, 87, 38, 16, 1, 0, 0
- Max VAF ≥0.1: 64, 34, 14, 5, 3, 1, 0
Results: Multivariate Cox regression for PFS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PFS HR (95% CI)</th>
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<tr>
<td>Pre-RT ctDNA Level (Maximum VAF) [p=0.0253]</td>
<td>3.781 (1.081–11.3)</td>
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<td>Gender (Female)</td>
<td>1.178 (0.7274–1.924)</td>
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<tr>
<td>Histology (Squamous) [p=0.0292]</td>
<td>1.984 (1.047–3.614)</td>
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<tr>
<td>Age at Diagnosis [p=0.0394]</td>
<td>1.024 (1.001–1.048)</td>
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<tr>
<td>Smoking Status</td>
<td>0.769 (0.4478–1.358)</td>
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<tr>
<td>Metastatic Organ Systems</td>
<td>0.9757 (0.6212–1.444)</td>
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<tr>
<td>Initial Stage</td>
<td>1.426 (0.8918–2.623)</td>
</tr>
<tr>
<td>Lines of Therapy [p=0.0001]</td>
<td>1.382 (1.161–1.625)</td>
</tr>
<tr>
<td>Select Mutations &amp; Alterations</td>
<td>0.7981 (0.4675–1.339)</td>
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Results: ctDNA levels don’t correlate well with # of metastatic organ systems

Correlation Between Metastatic Disease and Maximum VAF

Correlation Between Metastatic Disease and ctDNA Mutational Burden
These real-world data suggest that pre-treatment ctDNA could be a predictive biomarker for oligometastatic NSCLC treated with XRT.
Conclusions

• We have exciting real-world data suggesting that ctDNA detection and levels can risk-stratify oligometastatic NSCLC.
• Oligometastatic patients with low or undetectable ctDNA had improved survival outcomes with radiotherapy.
• While ctDNA correlated with survival outcomes, the number of metastatic disease sites did not.
• We need to test ctDNA-based decision frameworks for consolidation SABR/SBRT for oligometastatic disease in prospective clinical trials.