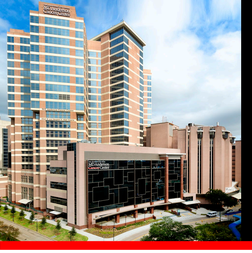


#003 THE EMERGING ROLE OF ctRNA IN LIQUID BIOPSY – INSIGHTS FROM TWO CLINICAL TRIALS IN ONCOGENE-DRIVEN NON-SMALL CELL LUNG CANCER

Simon Heeke[1], Saumil Gandhi[2], Hai Tran[1], Xiuning Le[1], Natalie Vokes[1], Mara Antonoff[3], Vincent Lam[4], Maliazurina Saad[5], Michelle Pek[6], Kao Chin Ngeow[7], Jia Wu[1,5], Jianjun Zhang[1], John Heymach[1], Yasir Elamin[1]

1 Department of Thoracic Head & Neck Medical Oncology, UT MD Anderson Cancer Center, Houston, USA. 2 Department of Radiation Oncology, UT MD Anderson Cancer Center, Houston, USA. 3 Department of Thoracic and Cardiovascular Surgery, UT MD Anderson Cancer Center, Houston, USA. 4 Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Baltimore USA. 5 Department of Imaging Physics, UT MD Anderson Cancer Center, Houston, USA. 6 Lucence Health, Palo Alto, USA. 7 Lucence Diagnostics, Singapore.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Background

- BRIGHTSTAR is a prospective clinical trial assessing the addition of Local Consolidative Therapy (LCT) in addition to Brigatinib in *ALK* fusion positive advanced NSCLC
- Detection of ALK fusions transcripts in plasma remains challenging
- **Can inclusion of ctRNA in a liquid biopsy assay improve detection of *ALK* gene fusions?**

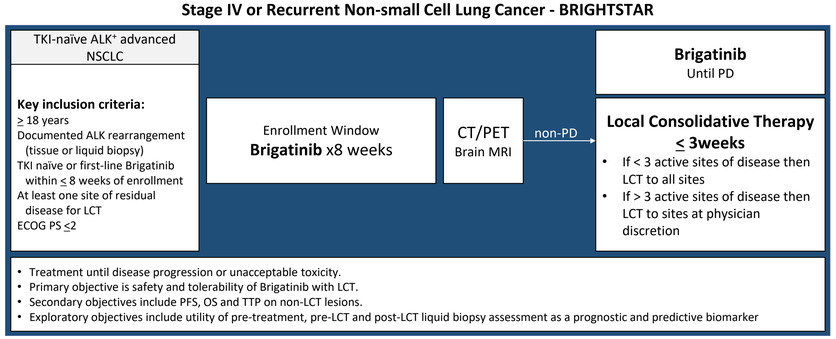
- CROSSOVER is a prospective clinical trial assessing the combination of Osimertinib with Alisertib or Sapanisertib in *EGFR* mutant NSCLC in patients who progressed after first line Osimertinib therapy
- **Can ctRNA expression guide selection and predict metastatic spread in *EGFR* mutant TKI-refractory NSCLC?**

Methods

- Liquid biopsy NGS assay analyzing 80 genes (including 32 analyzed by ctRNA) – LucenceHALLMARK (5ml plasma used)
- Analysis of 86 plasma samples from 33 patients in the BRIGHTSTAR trial at various timepoints. Baseline (N = 28), before LCT (N = 29), after LCT (N = 25), and at progression (N = 4)
- Analysis of 48 plasma samples from 38 patients in the CROSSOVER trial at various timepoints. Baseline (N=28), at cycle two of treatment (N=11) and at progression to treatment (N=9)

Results

Local Consolidative Therapy and Brigatinib in Treating Patients With Stage IV or Recurrent Non-small Cell Lung Cancer - BRIGHTSTAR



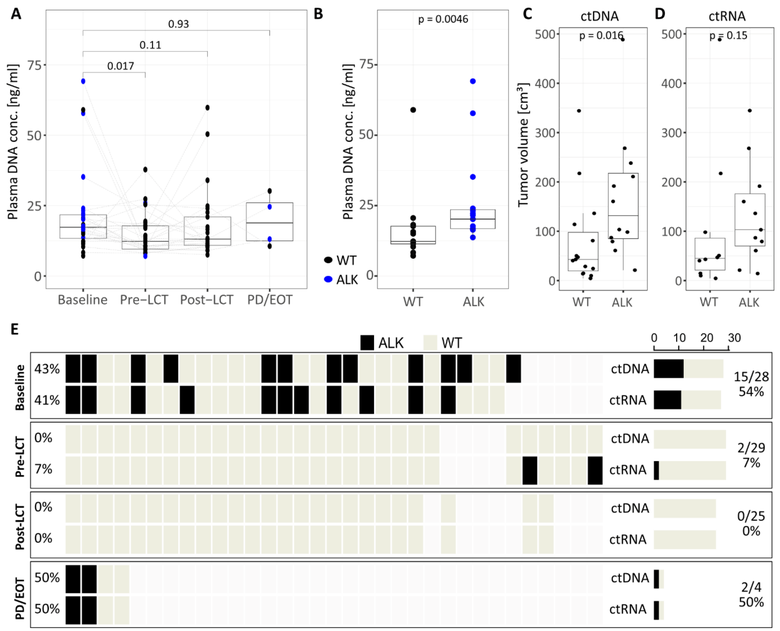


Figure 1: *Detection of ALK rearrangements using ctRNA and ctDNA. **A** Concentration of extracted DNA from plasma per timepoint in the BRIGHTSTAR clinical trial. **B** Differences in extracted plasma DNA for patients with detectable ALK rearrangement and those without detectable ALK rearrangement. **C** Differences in total tumor volume assessed by radiographic analysis and detection of ALK rearrangements at baseline using ctDNA and **D** ctRNA. **E** Overview on detection of ALK rearrangements at different timepoints in the full cohort.*

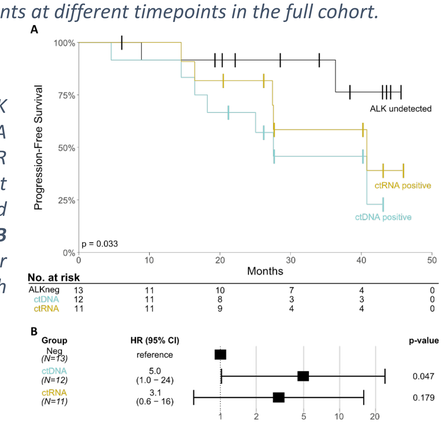
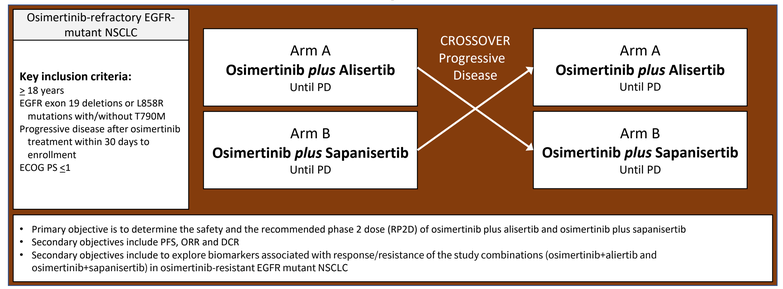


Figure 2: *Association of detection of ALK rearrangements with clinical outcome. A Progression-free survival for BRIGHTSTAR patients by detection of ALK rearrangement by ctDNA or ctRNA. Log-rank test for trend has been used to compute significance. **B** Cox proportional hazard ratio for association of ctDNA or ctRNA with progression-free survival.*

Osimertinib With Alisertib or Sapanisertib for the Treatment of Osimertinib-Resistant EGFR Mutant Stage IIIB or IV Non-Small Cell Lung Cancer - CROSSOVER



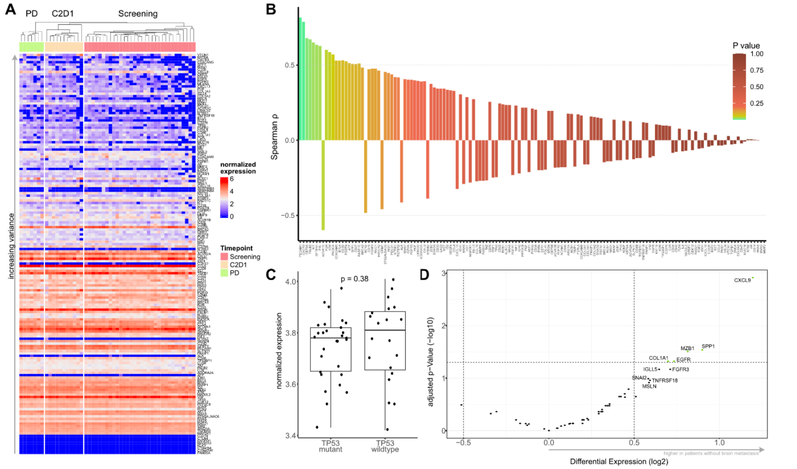


Figure 3: *Analysis of ctRNA expression in EGFR-mutant lung cancer. **A** Gene expression measured in ctRNA ordered by highest to lowest between samples variance is shown separated by timepoint. **B** Correlation of ctRNA expression with tissue RNA expression in matched samples at baseline. **C** Comparison of TP53 expression in ctRNA based on TP53 mutational status in all samples. **D** Differential expression of 50 most variable genes for patients with brain metastasis and patients without brain metastasis.*

Conclusion

- Inclusion of ctRNA improves detection of ALK rearrangements from plasma
- Baseline detection of ALK is associated with worse PFS
- ctRNA expression is associated with brain metastasis in EGFR TKI refractory NSCLC
- Clinical use of ctRNA expression requires further investigation