Background

- The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST; NCT02194738) was launched in 2014 across the National Clinical Trials Network (NCTN) of the National Cancer Institute (NCI).

- This trial platform aims to enroll up to 8,300 patients with resected high-risk non-small cell lung cancer (NSCLC) to facilitate enrollment to adjuvant targeted therapy trials following completion of standard adjuvant therapy.

- On 5/1/2016, the study was expanded to include squamous NSCLC and PDL1 testing to facilitate enrollment to a new immunotherapy study.

- Additionally, ALCHEMIST aims to collect biospecimens for clinical and investigational genomics.
**Methods and Study Design**

- Eligible patients have completely resected NSCLC, any histologic subtype, stage IB (≥4cm) to IIIA by AJCC 7.
- Eligibility window extends 75-285 days post-op depending upon receipt of adjuvant chemotherapy and/or radiation.
- Molecular testing of EGFR, ALK, PDL1 is performed centrally (depending on the histology and testing results) and results are returned to sites within 7-21 business days.
- FFPE tissue, whole blood, and plasma are collected at enrollment for genomic analysis.
- Appropriate patients may then enroll to one of three therapeutic trials studying single agent adjuvant targeted therapy (erlotinib NCT02193282, crizotinib NCT02201992, or nivolumab NCT02595944) versus observation.

**Diagram**

- Complete resection +/- standard adjuvant therapy per treating physician
- Non-squamous NSCLC
- Squamous NSCLC
- Specimen collection: FFPE tumor, whole blood, plasma
- PD-L1 testing
- EGFR & ALK genotyping
- EGFR-mutation: Phase III trial (A061105) - Erlotinib vs. observation
  - ALK-rearranged: Phase III trial (E4512) - Crizotinib vs. observation
  - PD-L1 pos/neg: Phase III trial (E45142) - Nivolumab vs. observation
- Not enrolled to treatment trial: Followed q6 months x 5 years after any adjuvant therapy
- FFPE tissue from biopsy submitted at recurrence
Follow Up

- This feasibility analysis was performed on patients enrolled as of April 29, 2019.
- 4,507 patients have been enrolled from 685 sites within the U.S.
- In the calendar year of 2018, median monthly enrollment to A151216 was 119 (range: 98-132).
- Central molecular testing was completed in 89.0%-92.7% of appropriate patients:
  - EGFR L858R/19del was detected in 560 of 3514 patients (15.9%).
  - ALK FISH was positive in 134 of 3,506 patients (3.8%).
  - PDL1 IHC was completed in 2,617 patients, and was >1% in 1,628 patients (62.2%).
- 3,304 patients were potentially eligible for the adjuvant treatment trials based upon molecular results and with sufficient post-surgical follow-up:
  - An additional 270 patients remained within the eligibility window for enrollment to treatment trial.
  - 1,089 patients (33.0%) were enrolled to a treatment trial.
  - Patients who enrolled were younger (p<0.01) and had higher N stage (p<0.01) than those not enrolled.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Enrolled (N=1089)</th>
<th>Not Enrolled (N=1945)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years*</td>
<td>66 (33 – 92)</td>
<td>68 (34 - 91)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>Female, Male</td>
<td>55%, 45%</td>
<td>53%, 47%</td>
<td></td>
</tr>
<tr>
<td>Tumor Size, cm²</td>
<td>3.7 (0-14)</td>
<td>4.0 (0.6-16.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pathologic T Stage</td>
<td></td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>T0, T1a, T1b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2a, T2b</td>
<td>41%, 15%</td>
<td>39%, 16%</td>
<td></td>
</tr>
<tr>
<td>T3, T4</td>
<td>19%, 3%</td>
<td>23%, 3%</td>
<td></td>
</tr>
<tr>
<td>Pathologic N Stage</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>N0, N1, N2</td>
<td>35%, 38%, 27%</td>
<td>41%, 38%, 22%</td>
<td></td>
</tr>
<tr>
<td>Clinical M Stage</td>
<td></td>
<td></td>
<td>0.51</td>
</tr>
<tr>
<td>M0, M1</td>
<td>100%, 0%</td>
<td>99.9%, 0.1%</td>
<td></td>
</tr>
</tbody>
</table>
Biospecimen Collection

- Adequate FFPE tissue and blood for advanced genomics was collected on 2859 of 4507 patients enrolled (63.4%):
  - Tumor sequencing is ongoing at the Genome Characterization Centers of the NCI's Center for Cancer Genomics, using multiple parallel sequencing platforms.
  - Following completion of the genomic analysis by study team, genomic data will be posted for public access.
- Plasma was collected at time of enrollment on 2006 patients enrolled since January 2017 (44.5% of all patients enrolled):
  - Plasma specimens can be used in the future for MRD studies, including analysis that are informed by tumor genomics or approaches that are agnostic to tumor sequencing results.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Analysis Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFPE slides for clinical genotyping</td>
<td>EGFR sequencing, ALK FISH, PDL1 IHC</td>
</tr>
<tr>
<td>FFPE block or scrolls for advanced genomics</td>
<td>Whole exome sequencing</td>
</tr>
<tr>
<td></td>
<td>Whole genome sequencing</td>
</tr>
<tr>
<td></td>
<td>RNA sequencing</td>
</tr>
<tr>
<td></td>
<td>miRNA sequencing</td>
</tr>
<tr>
<td>Whole blood</td>
<td>Paired germline for tumor genomics</td>
</tr>
<tr>
<td>Plasma and paired cell pellet (two Streck tubes)</td>
<td>Save for future studies of minimal residual disease (MRD) detection</td>
</tr>
<tr>
<td>FFPE tissue from recurrence biopsy (if available)</td>
<td>Comparison to initial resection specimen</td>
</tr>
</tbody>
</table>
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Adjuvant Targeted Therapy Following Standard Adjuvant Therapy for Resected NSCLC: An Initial Report from ALCHEMIST (Alliance A151216)

Geoffrey R. Oxnard¹, Sumithra Mandrekar², Shauna Hillman², Angelina Tan², Ramaswamy Govindan³

¹Dana-Farber Cancer Institute ²Alliance Statistics and Data Center, ³Washington University School of Medicine

Conclusions

- ALCHEMIST has achieved an enrollment of ~100 patients/month with resected high-risk NSCLC.
- This initial report demonstrates the feasibility of central molecular testing for enrollment to adjuvant targeted therapies.
- Only 36.3% of potentially eligible patients were enrolled to an adjuvant treatment trial with the primary reason being lack of interest in further adjuvant therapy.
- Enrollment continues toward the aim of using adjuvant targeted therapies to improve survival in high risk resected NSCLC.

Future Directions

- We are currently working to add additional treatment arms to replace those arms that complete enrollment.
- Tumor sequencing results offer a unique opportunity to rigorously assess the prognostic significance of a range of molecular features.
- We hope to use existing plasma to clinically validate MRD assays which could be prospectively studied in future NCTN studies.
Adjuvant Targeted Therapy Following Standard Adjuvant Therapy for Resected NSCLC: An Initial Report from ALCHEMIST (Alliance A151216)

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Background

Alliance A151216 is funded by the National Institutes of Health through National Cancer Institute grant awards.

- We appreciate the time and energy committed by patients and investigators across the NCTN.
- We especially want to acknowledge these 10 top enrolling sites to A151216 (as of 4/29/2019):

<table>
<thead>
<tr>
<th>Site</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moffitt Cancer Center</td>
<td>87</td>
</tr>
<tr>
<td>Saint Luke’s University Hospital-Bethlehem Campus</td>
<td>60</td>
</tr>
<tr>
<td>Rhode Island Hospital</td>
<td>53</td>
</tr>
<tr>
<td>University of Pittsburgh Cancer Institute (UPCI)</td>
<td>50</td>
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<tr>
<td>Duke University Medical Center</td>
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<tr>
<td>University of Michigan Comprehensive Cancer Center</td>
<td>45</td>
</tr>
<tr>
<td>Dana-Farber/Harvard Cancer Center</td>
<td>44</td>
</tr>
<tr>
<td>Roswell Park Cancer Institute</td>
<td>43</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>42</td>
</tr>
<tr>
<td>Memorial Sloan Kettering Cancer Center</td>
<td>41</td>
</tr>
</tbody>
</table>

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Funding Support

Acknowledgement

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