LUNG-MAP
Lung Master Protocol

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Disclosures: None
LUNGMAP Objectives

• **Title:** A Master Protocol to Evaluate Biomarker-Driven Therapies and Immunotherapies in Previously-Treated Non-Small Cell Lung Cancer (Lung-MAP Screening Study)

• **Primary Objectives**
  – Test patient specimens to determine eligibility for participation in the biomarker-driven and non-matched sub-studies included within the Lung-MAP umbrella protocol.

• **Secondary Objectives**
  – Screening Success Rate Objective
    • To evaluate the screen success rate defined as the percentage of screened patients that register for at therapeutic sub-study. Screen success rates will be evaluated for the total screened population and by the subset of patients screened following progression on previous therapy or pre-screened on current therapy.
  – Translational Medicine Objective
    • To evaluate circulating tumor DNA (ctDNA) and compare to the FMI Foundation tissue molecular profiling results in patients who submit a new biopsy for screening.
    • To establish a tissue/blood repository.
Summary of Screening Protocol-LUNGMAP

- Inclusion of all histologic types of NSCLC
- Expand to allow patients with known driver-mutations after progression on all standard of care targeted therapies.
- Inclusion of liquid biopsy:
  - At screening, for comparison with those undergoing fresh tissue biopsy
  - To all sub-studies
  - Assessment of TMB and allelic frequency (potential serial sampling for early prediction of outcome)
- PD-L1 testing on all patients

All sites must use the central IRB (cIRB)
Foundation One testing
Where are we now?

<table>
<thead>
<tr>
<th>As of 07/06/22</th>
<th>Total</th>
<th>S1400</th>
<th>LUNGMAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening Registrations</td>
<td>4432</td>
<td>1864</td>
<td>2568</td>
</tr>
<tr>
<td>Screened at PD</td>
<td>2070</td>
<td>1127</td>
<td>943</td>
</tr>
<tr>
<td>Pre-screened*</td>
<td>2362</td>
<td>737</td>
<td>1625</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sub-study Assignments</th>
<th>Total</th>
<th>S1400</th>
<th>LUNGMAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Among Screened at PD</td>
<td>1781</td>
<td>996</td>
<td>785</td>
</tr>
<tr>
<td>Among Pre-screened</td>
<td>954</td>
<td>414</td>
<td>540</td>
</tr>
<tr>
<td>Additional Assignments after PD on a Sub-study</td>
<td>121</td>
<td>74</td>
<td>47</td>
</tr>
</tbody>
</table>

Sub-study Registrations 1055

* pre-screening was added in May 2015 (11 months after activation)
** includes 21 pts registered to a LUNGMAP sub-study
S1900E Schema

Registration to Screening Study

KRAS$^{G12C}$-Positive non-squamous NSCLC by FMI

Sub-Study Assignment and Registration to S1900E

Cohort 1: co-mutation with TP53

Cohort 2: co-mutation with LKB1/STK11

Cohort 3: all others

AMG 510 to Progression

Accrual Goal: 132 patients
S1800D Schema

Prior Anti-PD-(L)1 and disease progression

PD on prior treatment ≤ 12 weeks

Primary Resistance Cohort

Stand-alone Phase II

N = 130

N-803 + Pembrolizumab

Standard of Care

Primary Endpoint: Overall Survival
Comparison: Weighted Log-rank test
Minimum Follow-up requirements for all analyses (interim and final)

PD on prior treatment > 12 weeks

Acquired Resistance Cohort

Phase II/III

N = 300

N-803 + Pembrolizumab

Standard of Care

Primary Endpoint: Overall Survival
Comparison: Standard Log-rank test
Minimum Follow-up requirements for all analyses (interim and final)

Standard of Care: Docetaxel + Ramucirumab, Docetaxel, Gemcitabine, Pemetrexed
Overall survival from a phase II randomized study of ramucirumab plus pembrolizumab versus standard of care for advanced non-small cell lung cancer previously treated with immunotherapy—Lung-MAP non-matched sub-study S1800A

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S1800A Schema—Randomized Phase II trial

NCT03971474

**Stratified by** 1) PD-L1 expression, 2) histology, 3) intent to receive ramucirumab in standard of care arm

**Primary endpoint:** OS

**Secondary endpoints:** RR, DCR, DoR, PFS, Toxicities

**ARM A**
Investigator’s Choice Standard of Care
docetaxel + ramucirumab;
docetaxel; gemcitabine;
pemetrexed (nonSCC only)

**Randomization**
R (1:1)
N= 130

**ARM B**
Pembrolizumab
200 mg Q3W for up to 35 cycles +
Ramucirumab
10 mg/kg Q3W

**Key eligibility:** 1) Previously received both PD-1 or PD-L1 inhibitor therapy and platinum-based doublet chemotherapy either sequentially or combined, with PD on at least 84 days after initiation of ICI and platinum-based doublet therapy; 2) ECOG 0-1; 3) all patients met eligibility to receive ramucirumab
Overall survival

- Median OS for RP 14.5 months v. SOC 11.6 months
- HR = 0.69; SLR p-value 0.05

Standard of care therapy received:
- Docetaxel + Ramucirumab (n = 45)
- Docetaxel (n = 3)
- Gemcitabine (n = 12)
- Pemetrexed (n = 1)
- No treatment (n = 6)
Acknowledgements

Lung-MAP Partners and Collaborators
Acknowledgements

Lung-MAP Impact

- Over 15 clinical trials following Lung-MAP blueprint
- FDA now has “master protocol” guidance and most pharma companies have launched a “master protocol”
- Over 4,000 registered patients at more than 900 sites
- Over 50 publications and abstracts
- Over 10,000 specimens in a public bank
- 300 genes identified with a genetic alteration

Most importantly, we are grateful Lung-MAP has helped many patients and we want to amplify our success so far by opening the trial to more patients!

I continue to be so grateful for everyone involved. Even after 48 visits for my opdivo infusion!
~ Annie B.

I am more confident than I have been in a long time. Lung-MAP gave me my life back. ~ Clifford C.