Lung Cancer Landscape

Challenges

- Silos of research with suboptimal sharing of data
- Stigmatized, under-funded research
- Inconsistent clinical care/multi-disciplinary engagement
- Under-enrolling clinical trials
- Incomplete understanding of disease drivers
- No early detection markers
- Ultimately ineffective therapies

Solutions

- Patient-centric...
  - services, support, and education
  - directed research
Lung Cancer Landscape

225,000

alive @5 yrs
17%

79%

Adv. Stage

alive @5 yrs
2%
A patient-focused translational research consortium: DRIVING PROGRESS

Accelerated, heightened impact:
- Tumor biology and therapeutics
- Portfolio of innovative projects
- Centralized study management and monitoring
- Consortium master agreement
- Centralized tissue bank
- Centralized data systems:
  - Electronic Data Capture
  - Remote consenting & screening
## ALCMI Consortium Members

<table>
<thead>
<tr>
<th>Region</th>
<th>Institution</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>North</strong></td>
<td>Dana-Farber Cancer Institute</td>
<td>Massachusetts, USA</td>
</tr>
<tr>
<td></td>
<td>New York University</td>
<td>New York, USA</td>
</tr>
<tr>
<td></td>
<td>Lahey Clinic</td>
<td>Massachusetts</td>
</tr>
<tr>
<td></td>
<td>Ohio State University</td>
<td>Ohio, USA</td>
</tr>
<tr>
<td><strong>South</strong></td>
<td>Vanderbilt University</td>
<td>Tennessee, USA</td>
</tr>
<tr>
<td></td>
<td>Memorial Cancer Institute</td>
<td>Florida</td>
</tr>
<tr>
<td></td>
<td>Boca Raton Regional Hospital</td>
<td>Florida</td>
</tr>
<tr>
<td></td>
<td>Northside Hospital</td>
<td>Georgia, USA</td>
</tr>
<tr>
<td><strong>West</strong></td>
<td>Alta Bates Summit Medical Center</td>
<td>California, USA</td>
</tr>
<tr>
<td></td>
<td>El Camino Hospital</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>Hoag Hospital</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>Palo Alto Medical Foundation</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>Tahoe Forest Cancer Center</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>University of California at Davis</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>University of California San Francisco</td>
<td>California</td>
</tr>
<tr>
<td></td>
<td>University of Southern California</td>
<td>California</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td>Institut Gustave Roussy</td>
<td>Paris, France</td>
</tr>
<tr>
<td></td>
<td>University of Torino</td>
<td>Turin, Italy</td>
</tr>
<tr>
<td></td>
<td>Catalan Institute of Oncology</td>
<td>Barcelona, Spain</td>
</tr>
<tr>
<td><strong>United Kingdom</strong></td>
<td>University of Manchester</td>
<td>Manchester</td>
</tr>
</tbody>
</table>
Scientific Leadership Board

Executive board selected from ≥60 ALCMI investigators

David P. Carbone, MD, PhD, Professor in the Division of Medical Oncology, Chair of ALCMI Scientific Leadership Board
Ohio State University

David R. Gandara, MD, Professor of Medicine, Associate Director of Clinical Research and Director of Thoracic Oncology
University of California, Davis

David M. Jelbian, MD, Professor & Chief of Thoracic Surgery, Ada Distinguished Professor of Thoracic Oncology, Program Leader of Thoracic Oncology at the UCSF Cancer Center
University of California San Francisco

Pasi A. Jänne, MD, PhD, Associate Professor of Medicine at Harvard Medical School; Scientific Director, Belfer Institute for Applied Cancer Science at Dana-Farber Cancer Institute
Dana-Farber Cancer Institute

He Liard-Offringa, PhD, Associate Professor of Surgery and of Biochemistry and Molecular Biology at Norris Comprehensive Cancer Center, Director of the Program in Biomedical and Biological Sciences
University of Southern California

Harvey I. Pass, MD, Professor of Thoracic Oncology, Vice-Chair Research, Department of Cardiology and Division Chief of General Thoracic Surgery
New York University

Rafael Rosell, MD, PhD, Scientific Director for Oncology, Chief of Medical Oncology Service at Hospital Germans Trias i Pujol; Chairman of Pangea Biotech, SA; Professor at University of Barcelona
Catalan Institute of Oncology (Spain)

Giorgio V. Scaglotti, MD, PhD, Chair and Professor of Respiratory Medicine, Professor of Thoracic Oncology
University of Torino (Italy)

Jean-Charles Soria, MD, PhD, Professor of Medicine and Medical Oncology at South Paris University
Institut Gustave Roussy (France)
INVESTIGATORS/SLB TELECONFERENCE
MARCH 30\textsuperscript{TH} or 31\textsuperscript{ST}, 2015
(RSVP to syoung@alcmi.net)

CONFERENCE DIAL-IN: you may use your computer audio & view shared documents via
(https://www.uberconference.com/alcmi), and also dial-in via telephone (below):
- France (16:00-17:00): 01 82 88 57 11, when prompted enter U.S. number below followed by #
- Italy (16:00-17:00): 06 9480 3156, when prompted enter U.S. number below followed by #
- United Kingdom (15:00-16:00): 020 3514 1993, when prompted enter U.S. number below followed by #
- United States (7-8 am PST/9-10 am CST/10-11 am EST): 1 866 308 7444

Agenda

I. Bonnie J. Addario Lung Cancer Foundation Update

II. March Spotlight:
- Group Discussion: blood-based assays and ALCMI collaboration opportunities
  - introductory overview/slides by D. Carbone
  - slides emailed separately, but also will be shown live via https://www.uberconference.com/alcmi
  - see page two below for CASTLE study schema

III. ALCMI Research:
- A. New Projects in Development:
  - Epidemiology of Lung Cancer in Young Patients

- B. Initial Study Ideas:
  - Opportunities: BMS (ImmunoTx), Merck (ImmunoTx), Guardant Health (plasma NGS), Myriad (HRD (homologous recombination DNA repair assay), VisionGate3D (sputum, screening), Biocept (cfDNA, CTCs), LifeTell (blood immunosignatures), Verastem (stem cells)
Blood-Based Biomarkers to Guide Treatment of Advanced NSCLC

David P. Carbone, MD, PhD
Director, James Thoracic Center
The Ohio State University Wexner Medical Center
Columbus, OH
Blood-Based Biomarkers

- Many being developed, several are clinically available now
- Sources for blood-based biomarkers:

New Study: Liquid Biopsies/Analyses

Launch: ~Q4 2015

Support evolution from:

• single point mutations to comprehensive genomic profiling of blood (circulating tumor cells and DNA, exosomes (RNA)) and urine (RNA/DNA)

• genetic description to genomic action-ability

• diagnostic dependency on symptoms to early detection

• sporadic to near real-time disease progression and acquired resistance monitoring

• late to early stage detection and intervention
Accelerating the discovery, development and delivery of advancements to patients.

I. **CASTLE:** clinical, molecular and outcomes data with matched, serial biospecimens from advanced lung cancer patients: 140 enrolled (~5,500 specimens)
   - Response Genetics Inc.
   - Biodesix Inc.
   - Exosome Diagnostics
   - NeoStem Oncology
   - Plus 4-6 other molecular testing laboratories

II. **INHERIT EGFR T790M:** prospective study on germline biology in high-risk families: 48 enrolled (23 families)  
    - Laboratory for Molecular Medicine

III. **Genomics of Young Lung Cancer:** comprehensive genomic profiling of young lung cancers: 53 enrolled
    - Foundation Medicine Inc.
Lung Cancer Landscape

- AdenoCA: 62%
- Squamous: 20%
- Small Cell: 13%
- Other: 5%

Genetic Changes:
- K-ras
- EGFR

1984:
- K-ras
- EGFR

2004:
- K-ras
- EGFR

2015:
- K-ras
- EGFR

Other genetic markers:
- KRAS
- ALK
- EGFR (other)
- HER2
- MEK1
- NRAS
- MET
- BRAF
- >1 gene
CASTLE Study: Overview

Launched 2010

**Hypothesis:**
Understanding the biology of lung cancer in advanced disease provides discovery insights into all stages of disease

**Study Plan:**

I. Prospectively, longitudinally collect tumor, blood (plasma, serum, circulating tumor cells, RNA/DNA) and annotating clinical data

II. Focus on patients in community setting

✓ 140 enrolled / additional 70 screened (as of March 2015)

**Key Differentiators:**

- Molecular testing, community access
- Rational therapeutic decisions/improved outcomes
- Partnerships with biopharmaceutical and diagnostics companies
CASTLE Study Overview

Longitudinal biobanking/data study with matched tissues, plasma, serum, RNA, DNA, & CTCs

- Focus on unmet needs:
  - Covered molecular (CLIA) testing
  - Unique, annotated biorepository from community & academic centers
- Successful, flexible platform for collaborations
  - Academia – discovery & development
  - Industry – diagnostics & therapies
CASTLE Study: Biospecimens

Fully annotated (including outcomes)

Tumor Tissue

Plasma, CTCs, ctDNA

Urine

Serum

RESPONSE GENETICS

diagnostic

Molecular Testing

research

ResponseDX* (or other CLIA labs)

Biorepository

biodesix

predictive

Molecular Testing

Research

VeriStrat

Biorepository

* ResponseDX Comprehensive Lung Profile
  - Sanger: EGFR; FISH: ALK, ROS1, RET, MET, FGFR1
  - NGS: ERBB2 (HER2), BRAF, DDR2, KRAS, ALK, AKT1, HRAS, JAK2, KDR, MAP2K1, NOTCH1, NRAS, NTRK1, NTRK2, NTRK3, PIK3CA, PIK3R1, PIK3R2, PTEN, PTPRD, CDKN2A, TP53
  - RNA expression: ERCC1, TS1, RRM1, EGFR, cMET
INHERIT EGFR T790M Study

Launched 2013

Hypothesis:
Understanding underlying biology in high-risk families will provide insight into why lung cancer occurs in never-smokers

Study Plan:
I. Prospectively identify patients with germline T790M in collaboration with CLIA labs and high volume cancer centers
II. Prospectively collect patient tissue, blood and CT scans
III. Recruit and study patient family members

✓ 60 enrolled from 22 families (as of March 2015)

Key Differentiators:
• Molecular testing and genetic counseling
• Creates registry of high-risk families
• Ability to study other rare populations
Underlying biology in high-risk families; factors causing lung cancer unrelated to smoking

- **Patient Benefit**: genetic counseling, early detection, familial risk stratification, patients directed to targeted trials and therapies, remote screening (www.dana-farber.org/T790Mstudy)

**Three Study Groups**

- **Cohort 1**: Have a cancer harboring *EGFR T790M* (excluding acquired T790M)
- **Cohort 2**: Are a first- or second-degree relative of a known germline carrier
- **Cohort 3**: Already known to carry a germline *EGFR* mutation on prior testing
**Hypothesis:** Lung cancer in younger patients different than in older patients

**Study Plan:**

I. Focusing on patients initially diagnosed under 40 years old

II. Prospectively collect and sequence new specimens and patient outcomes/clinical data

✓ First two weeks: 25 consented

**Key Differentiators:**

- First to prospectively characterize the somatic and germline genomics of young lung cancer across US, UK and Europe
- Clinical characteristics with an increased chance for a targetable mutation (e.g. never-smoking, adenocarcinoma histology)
- Individualized referrals to approved agents and clinical trials
To determine whether young lung cancers harbor a distinctive spectrum of genomic mutations

✓ Patient Benefit: no charge testing, prospective design, remote consenting/participation, identifying individualized management stratagems

• Initially diagnosed <40 years old:
  ✓ First to comprehensively map clinical genomics
  ✓ 3-6k diagnosed annually (US), requires innovative enrollment

M+ = any of mutations: EGFR, KRAS, HER2, BRAF, or rearrangements: ROS1, ALK, RET; F1 = Foundation One; Heme = FoundationOne Heme
The Connected Patient

- SMS text
- e-mail
- Fax
- Smart phone/iPad
- Mobile/remote devices
- Voice/Telephone
- Backend systems
- Web
GoYLC: Bringing the Study to the Patient

- Online recruitment
- Online consenting
- Remote sample handling
- Remote follow-up
- Site coordination

https://www.openmednet.org/site/alcmi-goyl
Remote Consenting & Participation

https://www.openmednet.org/site/alcmi-goyl

GENOMICS OF YOUNG LUNG CANCER STUDY

Lung cancer at any age is a catastrophic illness but it is particularly devastating when it affects young adults in the prime of their life. In other cancers, such as breast cancer and leukemia, research has clearly demonstrated that occurrence at a younger age is associated with a distinct biology that guides treatment. Thus, development of a unique treatment approach for young lung cancer is needed. The reason lung cancer occurs in young adults is not clear and this question has never been formally studied.

Click on a topic below for more information.

- Study Objectives and Eligibility
- Real Time Results Will Help Guide Treatment Options for Participants
- Discovery of a New Genetic Sub-Type of Lung Cancer
- A Fresh Look at the Germline Genetics of Lung Cancer Risk
- How to Participate
Remote Consenting & Participation

Prestudy
- Summit
- Study devel.
- Pre-Screening

Launch
- Remote sites
- Social media

Expansion
- Local Sites: US, UK, Italy
- Epidemiology

Science
Study Participation as of March 2015
(remote = ~70% of consented participants)

https://www.openmednet.org/site/alcmi-goyl
Driving Towards Goals

Diagnosis & Monitoring
- Screening/bio-monitoring
- Comprehensive profiling:
  - Diagnostic, prognostic, predictive

Innovative Trials
- Rational, profile-informed
- Patient engagement
- Remote trials, Big Data,...

Effective Therapies
- Personalized care plans
- Combo “cocktails”:
  - Targeted/immuno/...
- Payors engaged
“Always, always, think outside the box.”
THE “LIVING ROOM”
BRINGING HOPE HOME – PATIENT EDUCATION PROGRAM

• 600,000+ views in 143 Countries
• Video Library available 24/7 on-line
• Spanish Subtitles available on-line
• Spanish Speaking Living Room – May 12
• Mandarins Subtitles - Q4- 2015
• 10,000+ Hardcopies Distributed & On-line Downloads
• Available on Amazon.com
• Spanish version May 2015
• Mandarin version Q4 - 2015
10 ALCF COE sites:
Baptist Hospital, Memphis, TN
Dallas Presbyterian, Dallas, TX
El Camino Hospital, Mountain View, CA
Florida Hospital, Tampa, FL
Gibbs Cancer Center, Gafney, SC
Gunderson Hospital, LaCrosse, WI
Memorial Regional Hospital, Hollywood, FL
Moore Regional Hospital, Pinehurst, NC
St. Thomas Hospital, Nashville, TN
Tahoe Cancer Center, Truckee, CA

6 COE Sites w/MOU -30-60 days

11 COE Sites in discussion 90-120 days

COE Data Collection Database launch Q2 2015
ALCF Patient Caregiver Advisory Board (PCAB)

- Launched February 2015
- 11 Members
- 10 Patients
- 1 Caregiver
- 2 Initiatives in the works
AYA Speakers Live Stream Series
February 26, 2015
Topic: Genomics of Young Lung

May 5, 2015
Topic: Is Lung Cancer Inherited?

October 215
Topic: Young Adult Advocacy Panel Discussion: Collaboration
CLINICAL TRIALS ACCESS

- 44 Submissions YTD
- 5 International Submissions
- 3 Team Submissions

clinical trial INNOVATION PRIZE

A collaboration between Free to Breathe and the Bonnie J. Addario Lung Cancer Foundation.
Neutral-Branded National Awareness Initiative
A collaboration of 15 Lung Cancer Groups
Led by ALCF

Comprehensive Genomic Profiling