

Addario Lung Cancer Medical Institute

New Horizons

May 2015

Steven Young, President & COO
Addario Lung Cancer Medical Institute
(203) 226-5765, syoung@alcmi.net

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



BONNIE J. ADDARIO
LUNG CANCER
FOUNDATION



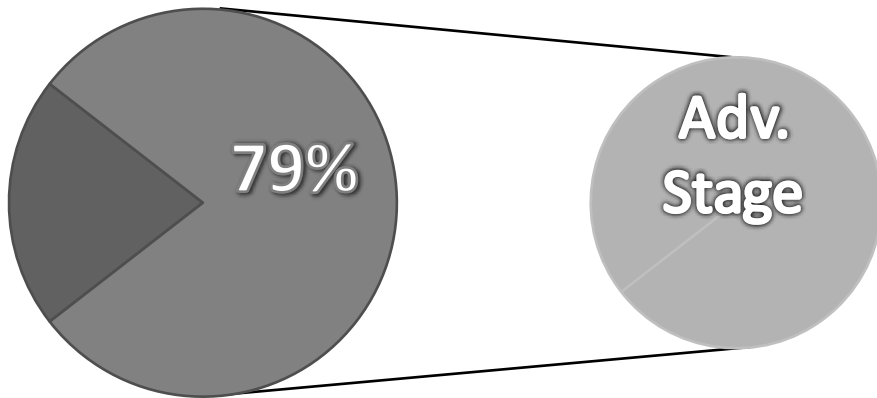
Lung Cancer Landscape

225,000

alive @5 yrs

552,000

17%

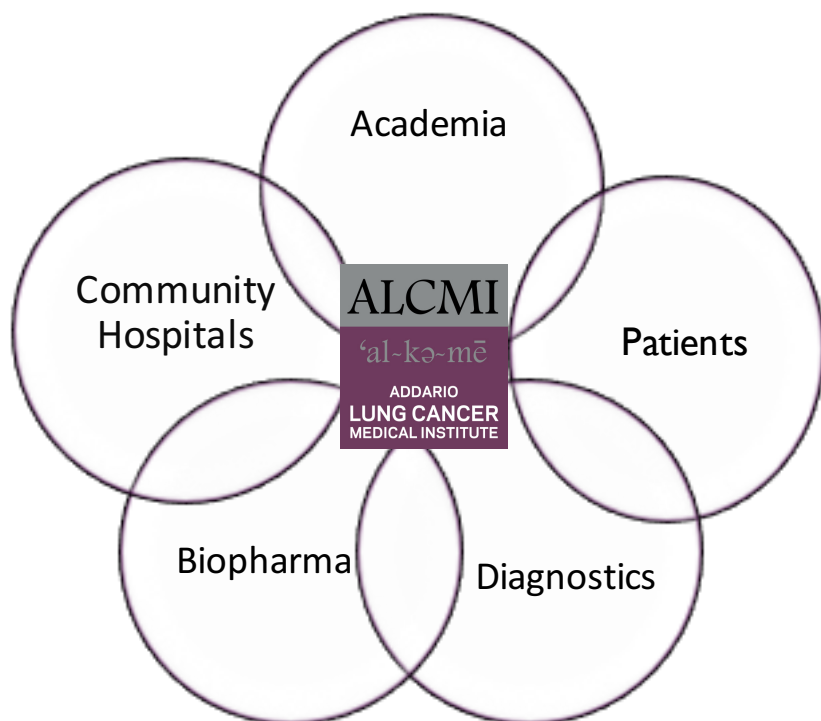


alive @5 yrs

2%

Founded in 2008

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

ALCFMI Consortium Members



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

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. Jablons, 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](#)



Ite Laird-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 Pangaea Biotech, SA; Professor at University of Barcelona
[Catalan Institute of Oncology \(Spain\)](#)



Giorgio V. Scagliotti, 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 30TH or 31ST, 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 3196, 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

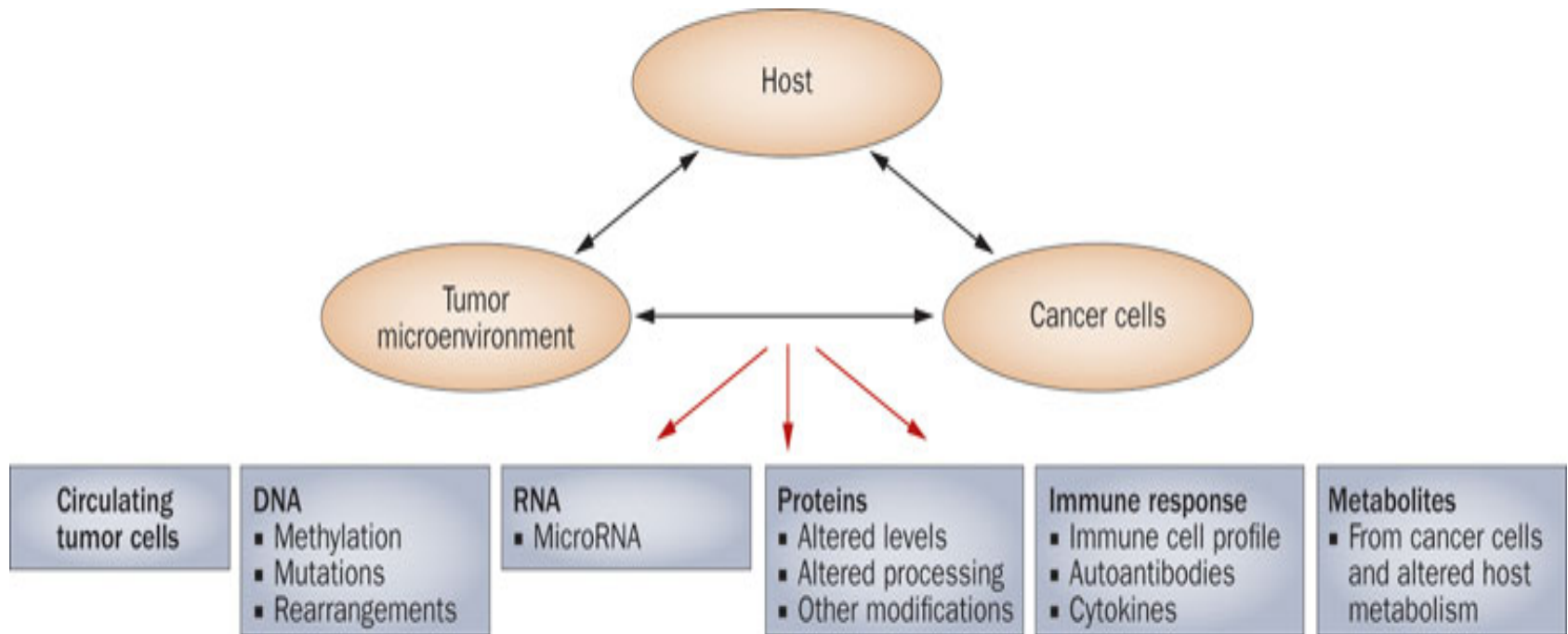
The Ohio State University Wexner Medical Center

Columbus, OH



Blood-Based Biomarkers

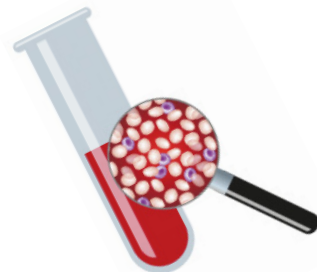
- Many being developed, several are clinically available now
- Sources for blood-based biomarkers:



Launch: ~Q4 2015

Support evolution from:

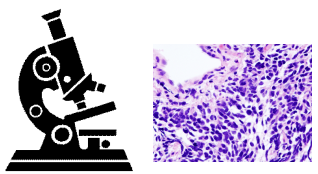
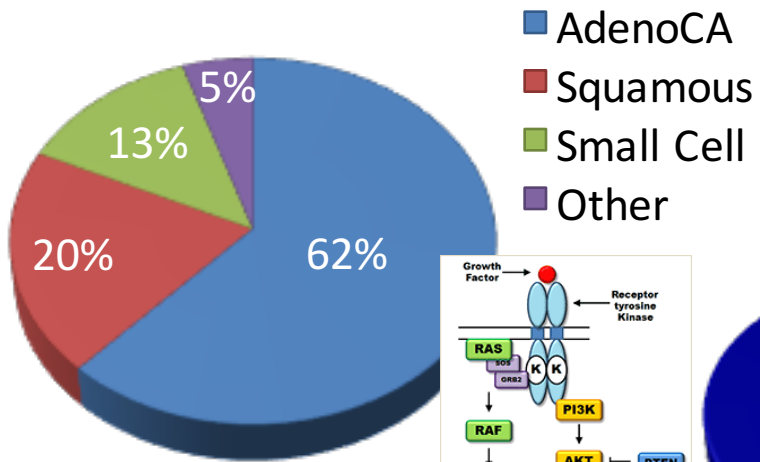
- **single point mutations to comprehensive genomic profiling of blood (circulating tumor cells and DNA, exosomes (RNA)) and urine (RNA/DNA)**
- **genetic description to genomic action-ability**
- **diagnostic dependency on symptoms to early detection**
- **sporadic to near real-time disease progression and acquired resistance monitoring**
- **late to early stage detection and intervention**



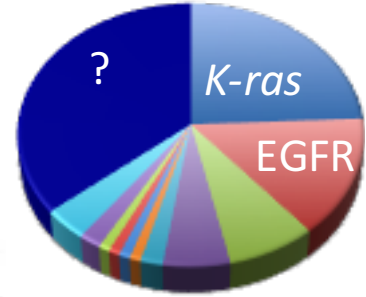
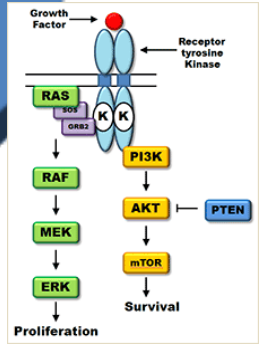
Accelerating the discovery, development and delivery of advancements to patients.

- 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)** **ASCO 2015**
 - ✓ Laboratory for Molecular Medicine
- III. **Genomics of Young Lung Cancer:** comprehensive genomic profiling of young lung cancers: **53 enrolled** **AACR & ASCO 2015**
 - ✓ Foundation Medicine Inc.

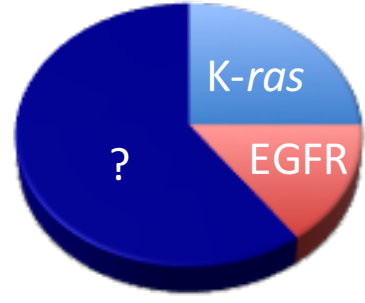
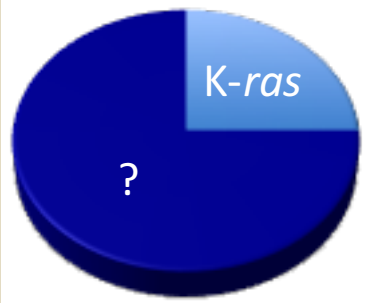
Lung Cancer Landscape



- AdenoCA
- Squamous
- Small Cell
- Other



- KRAS
- EGFR
- ALK
- EGFR (other)
- HER2
- MEK1
- NRAS
- MET
- PIK3CA
- BRAF
- >1 gene
- ?



1984

2004

2015



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

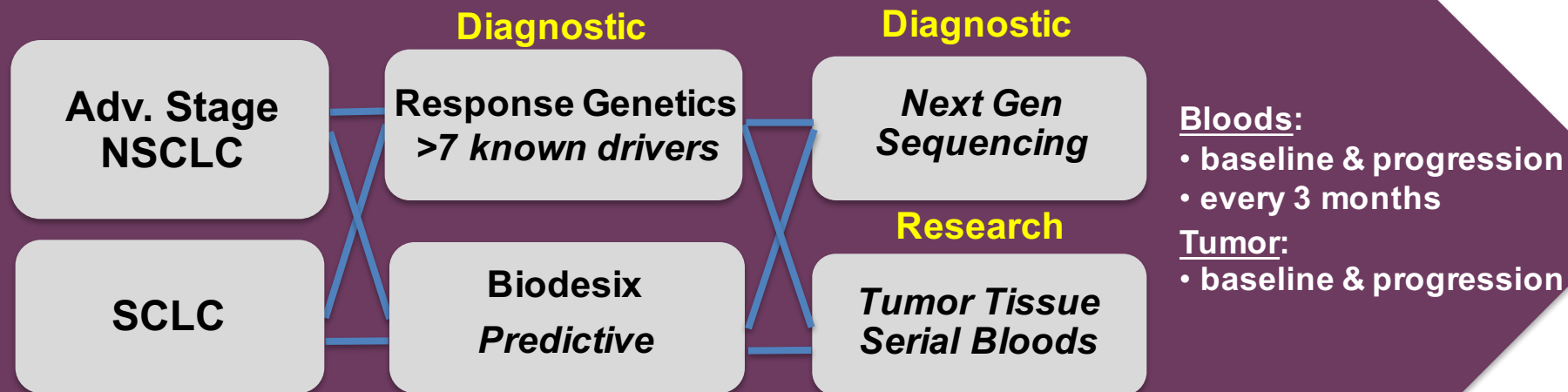
✓ **140 enrolled / additional 70 screened** (as of March 2015)

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

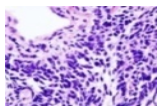


- **Focus on unmet needs:**
 - ✓ Covered molecular (CLIA) testing
 - ✓ Unique, annotated biorepository from community & academic centers
- **Successful, flexible platform for collaborations**
 - ✓ Academia – discovery & development
 - ✓ Industry – diagnostics & therapies

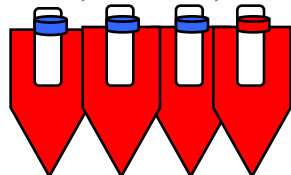
CASTLE Study: Biospecimens

Fully annotated (including outcomes)

Tumor Tissue



Plasma, CTCs, ctDNA



Urine

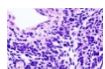


Serum



RESPONSE GENETICS

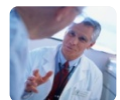
diagnostic



research

Molecular Testing

Research



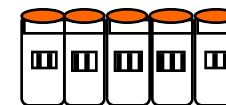
ResponseDX* (or other CLIA labs)



Biorepository

biodesix

predictive



research

Molecular Testing

Research



VeriStrat



Biorepository

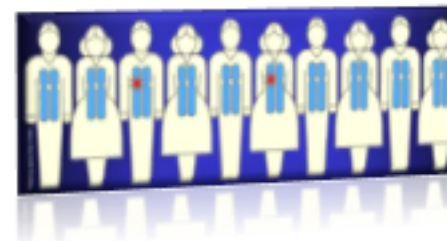
* ResponseDX Comprehensive Lung Profile

- 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

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

Counseling
re:
germline
testing

CLIA
testing
of saliva

Counseling
re: results

Confirm
positive
results by
testing
blood

Counseling
re: inviting
relatives

Collect
CT
imaging
&
follow for
2 years

- 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

Launched July 23, 2014

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

GENOMICS OF YOUNG LUNG CANCER STUDY

"The reason lung cancer occurs in young adults is not clear and this question has never been systematically studied (until now)."

—Bonnie J. Addario

Young Lung Cancer Deserves Focused Study to Facilitate Distinct Management Approach

- Lung cancer at any age is a catastrophic illness, but it is particularly devastating when it affects a young adult 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.
- Development of a unique treatment approach for young lung cancer patients – those under 40 years old at diagnosis – is needed.



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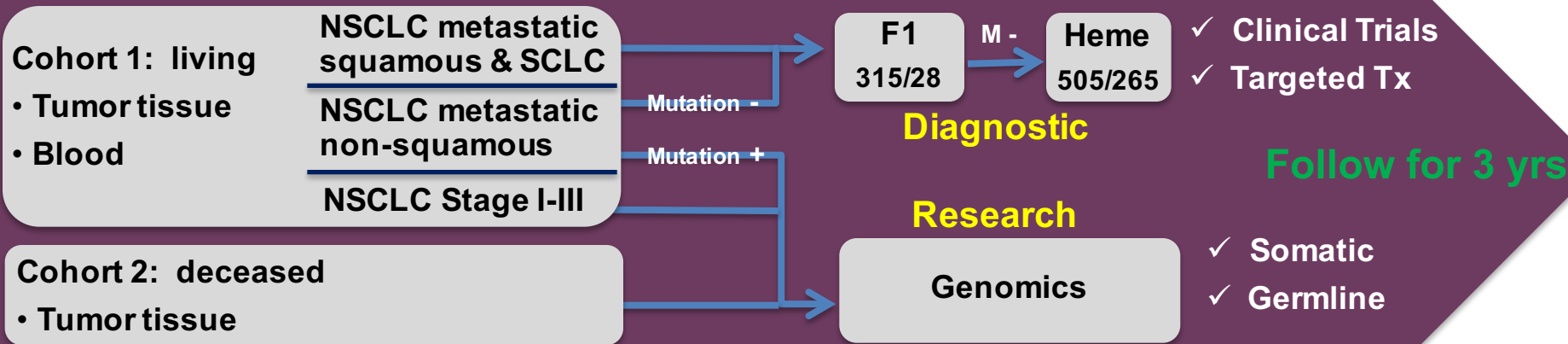
DISCOVERY OF A NEW GENETIC SUB-TYPE OF LUNG CANCER

REAL TIME RESULTS WILL HELP GUIDE TREATMENT FOR

Genomics of Young Lung Cancer

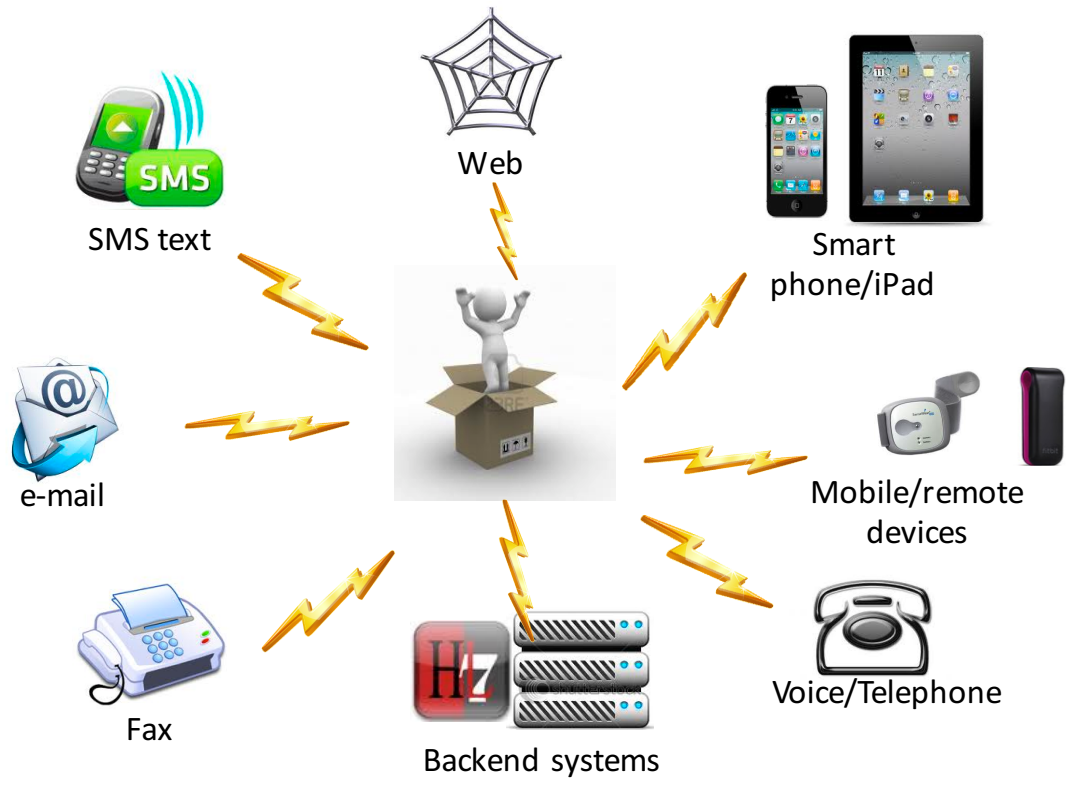
To determine whether young lung cancers harbor a distinctive spectrum of genomic mutations

- ✓ **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

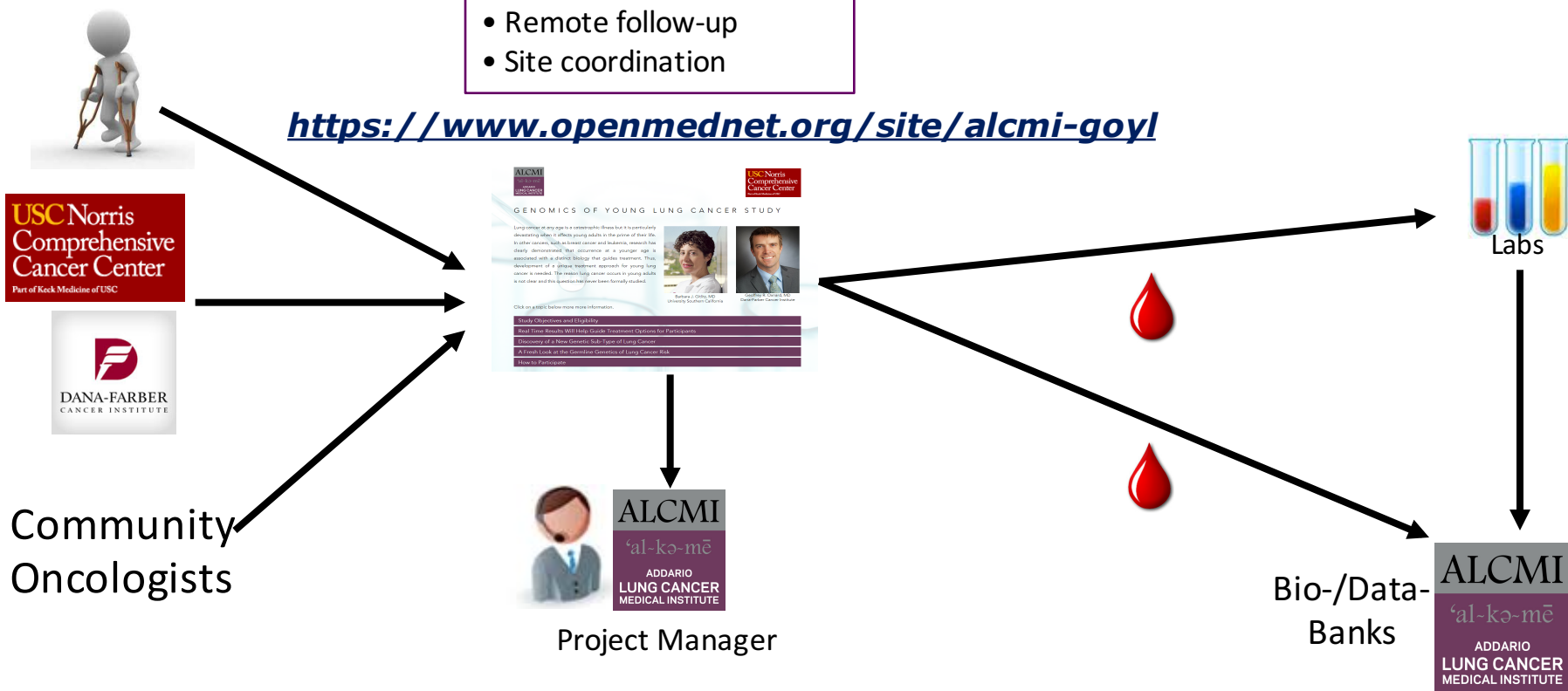
The Connected Patient



GoYLC: Bringing the Study to the Patient

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

<https://www.openmednet.org/site/alcfmi-goylc>



Community
Oncologists

USC Norris
Comprehensive
Cancer Center
Part of Keck Medicine of USC



ALCFMI
ADDARIO
LUNG CANCER
MEDICAL INSTITUTE

USC Norris
Comprehensive
Cancer Center

GENOMICS OF YOUNG LUNG CANCER STUDY

Lung cancer at any age is a heterogeneous illness but it is particularly devastating when it affects young adults. In the course of this study, further research, such as tumor cancer and genomic, research has clearly demonstrated that occurrence of a younger age is associated with a genetic biology that guides treatment. Thus, development of a clinical treatment approach for young lung cancer is needed. The reason lung cancer research in young adults is not clear and this question has been formally studied.

Click on a graphic below for more information:

- Study Objectives and Eligibility
- How This Research Will Help Guide Treatment Options for Participants
- Discovery of a New Genetic Sub-Type of Lung Cancer
- A Fresh Look at the Genetic Genetics of Lung Cancer Risk
- How to Participate



Project Manager



Labs

Bio-/Data-
Banks

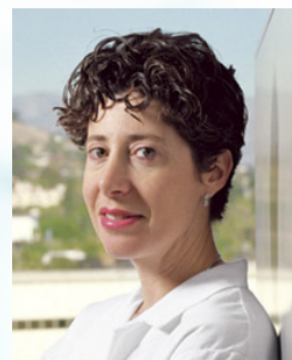


<https://www.openmednet.org/site/alcmi-goyl>



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.



Barbara J. Gitlitz, MD
University Southern California



Geoffrey R. Oxnard, MD
Dana-Farber Cancer Institute

Click on a topic below more more information.

Study Objectives and Eligibility

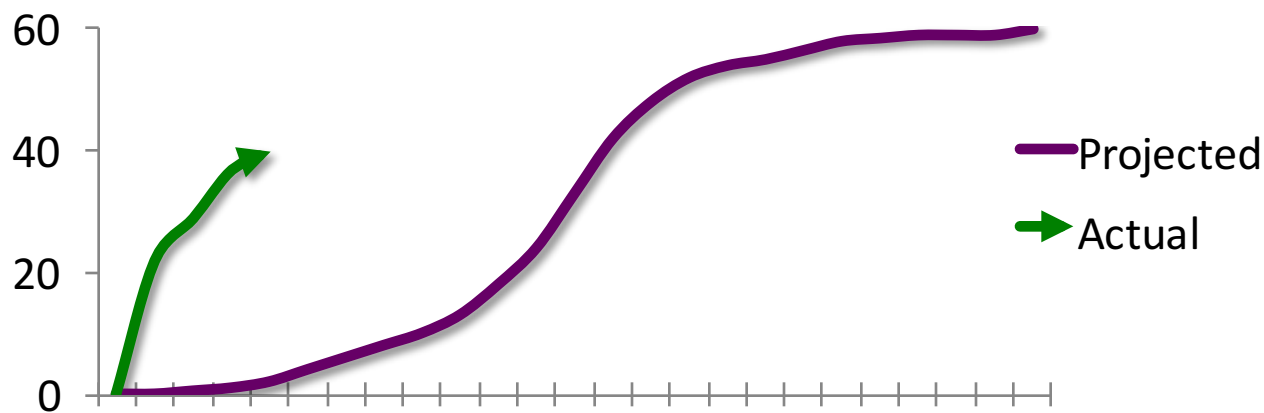
Real Time Results Will Help Guide Treatment Options for Participants

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



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Launch

Remote sites

Social media



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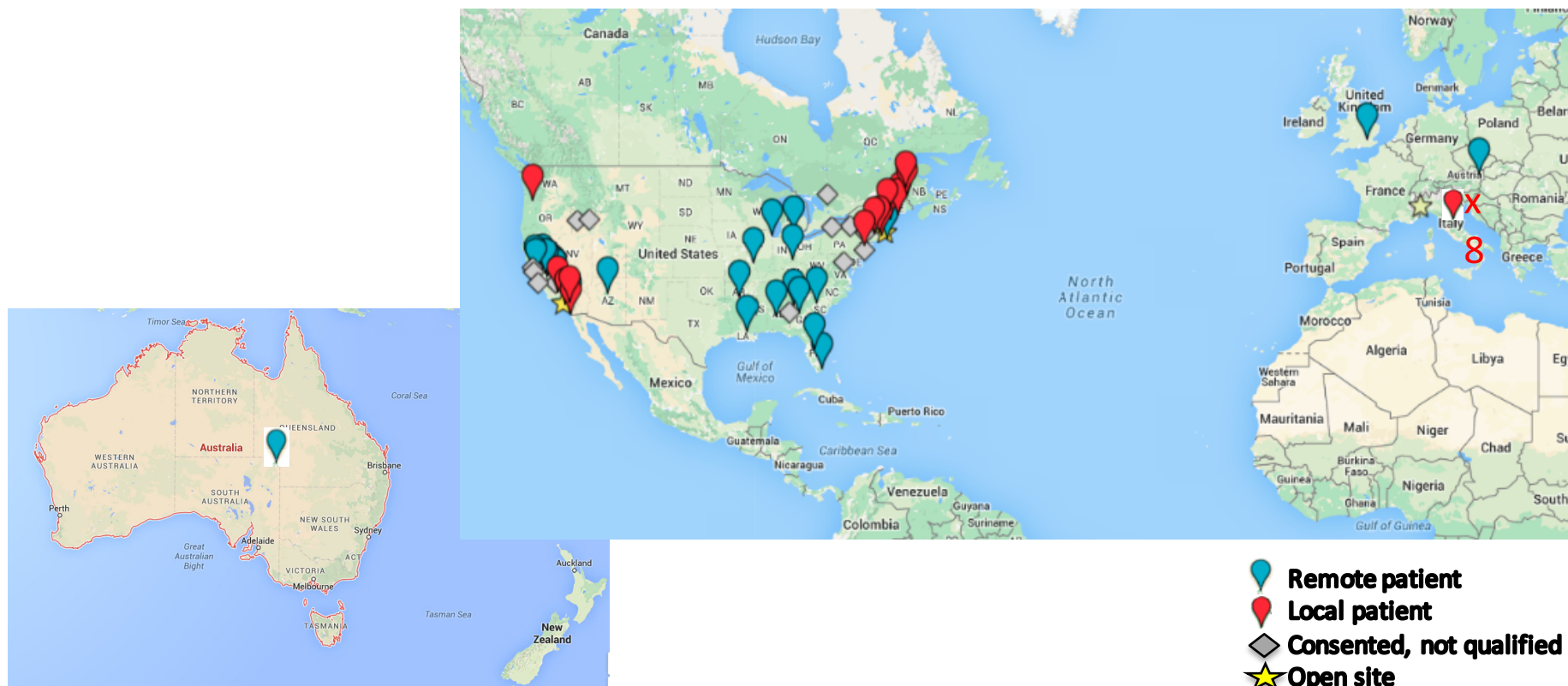
Expansion

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

Science

Study Participation as of March 2015

(remote = ~70% of consented participants)



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



RESPONSE
GENETICS



biodesix



PARTNERS
HEALTHCARE

CENTER FOR PERSONALIZED
GENETIC MEDICINE



NeoStem



FOUNDATION
MEDICINE®



OpenMedicine
INSTITUTE



GUARDANT HEALTH



BROAD
INSTITUTE





"Always, always, think outside the box."



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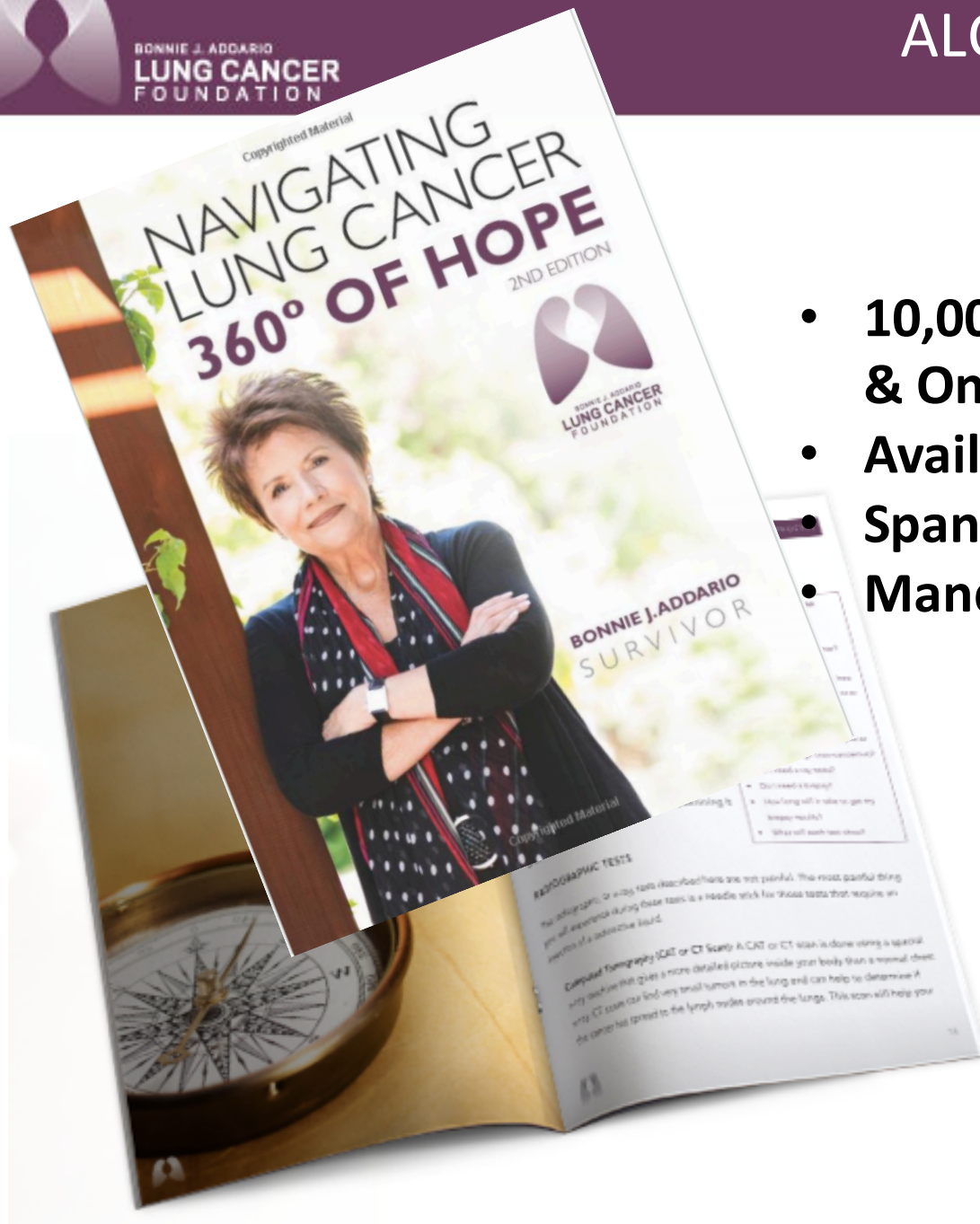
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livestream



- **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 sties:

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



- 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?

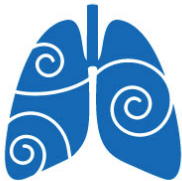
October 215

Topic: Young Adult Advocacy Panel Discussion:
Collaboration





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free to breathe
a partnership for lung cancer survival



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



WWW.LUNGCANCERFOUNDATION.ORG



@TheALCF

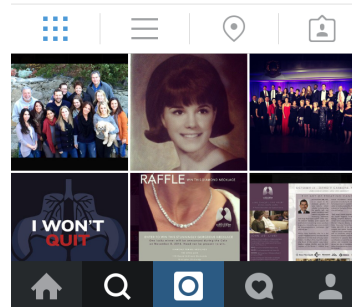


57 posts 373 followers 713 following



Addario Lung Cancer Foundation
ALCF is one of the largest patient-driven philanthropies nationwide devoted exclusively to eradicating Lung Cancer. Visit our website for more details
www.lungcancerfoundation.org

#beatlungcancer



Instagram

Neutral-Branded National Awareness Initiative
A collaboration of 15 Lung Cancer Groups
Led by ALCF

IF YOU HAVE LUNG CANCER
DON'T GUESS. TEST.

Comprehensive Genomic Profiling