Health Disparities in Lung Cancer in 2015

The Role of Primary Care in Reducing Cancer Disparities
March 28, 2015

The James
Ohio State is a Comprehensive Cancer Center designated by the National Cancer Institute

NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute
Disclosures

- Funding National Cancer Institutes
- Editorial Boards
  - Journal of Thoracic Oncology
  - American Journal of Respiratory and Critical care Medicine
Case Presentation

- 56 year old African American male presents for discussion regarding new diagnosis of advanced stage NSCLC
- PMHx: DM, HTN
- SocHx 40 pack year active smoker, no drugs no ETOH
- FamHx: positive for prostate cancer, HTN
- Examination: decreased breath sounds bilaterally, otherwise unremarkable
- He has been reading about genetic testing of tumors and is enquiring about his prognosis and best treatment options

How do you counsel him?
Challenges in Lung Cancer Diagnosis and Treatment

- How do we screen for lung cancer?
- How do we identify “early disease”?
- Are we staging patients correctly?
- Further characterizing the molecular heterogeneity in lung cancer—Biomarkers and targeted drugs
- Clinically relevant biomarkers (sputum, blood, CT, tumor?)
- Is lung cancer in non-smokers a different disease?
Lung Cancer in the United States

<table>
<thead>
<tr>
<th>New Cases</th>
<th>Rank</th>
<th>Deaths</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>228,190</td>
<td>2</td>
<td>159,480</td>
<td>1*</td>
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</tbody>
</table>

*More deaths than prostate, breast and colon cancer combined; 85% of lung cancer is NSCLC

Number of prevalence cases expected to reach 338,000 by 2030
How Much Progress Have We Made?

Despite large improvements for leukaemia (9-fold) and myeloma (6-fold), the median survival time still remains low with patients diagnosed in 2007 predicted median survival time at 3 and 2 and half years respectively.
Lung Cancer in Ohio

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>27%</td>
<td>9%</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td>17%</td>
<td>32%</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>10%</td>
<td>9%</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin's Lymphoma</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3%</td>
<td>6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
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<tr>
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<td>15%</td>
<td>27%</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Uterine Corpus &amp; Uterine NOS*</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin's Lymphoma</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Ovary</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3%</td>
<td>6%</td>
</tr>
</tbody>
</table>
Predicted Rates of Lung Cancer among Men Who Currently Smoke 10 Cigarettes per Day (Panel A) or 30 Cigarettes per Day (Panel B) and among Women Who Currently Smoke 10 Cigarettes per Day (Panel C) or 30 Cigarettes per Day (Panel D).

Disparities in Lung Cancer Incidence
Lung Cancer Death Rates

AA men are ~30% more likely to be diagnosed with lung cancer than Caucasians

Source: Centers for Disease Control
Geographical distribution

Cases from 2004-2006 (623,388)
Black men had highest incidence rates and younger age
Source: CDC and SEER

Underwood et al., Cancer, 2012
Histological differences

Lower overall mortality among HW
HW more represented in BAC
NHF: normalized histological frequency
Limited info on SES, chemo, occupation, smoking

Saeed et al., Cancer, 2012
Issues Driving Health Disparities in Lung Cancer

- Awareness
- Accessing the health care system/early presentation/rapid diagnostics
- Overcoming cultural biases towards tobacco consumption
- Early detection strategies
- Improve understanding and targeting of molecular risks
- Clinical trial enrollment
Addressing Disparities in Lung Cancer Care Objectives

- Early Detection
- Cultural Competency Awareness Outreach
- Smoking Cessation
- Survivorship
- Clinical Trials Mutational Analysis
- Access Rapid Diagnostics Navigation
Perceptions Regarding Lung Cancer

<table>
<thead>
<tr>
<th>HINTS Questions</th>
<th>% of Respondents</th>
<th>White</th>
<th>Black</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are so many different recommendations about preventing lung cancer</td>
<td></td>
<td>37</td>
<td>53</td>
<td>.021</td>
</tr>
<tr>
<td>Reluctant to get checked for lung cancer for fear that you may have it</td>
<td></td>
<td>9</td>
<td>22</td>
<td>.003</td>
</tr>
<tr>
<td>Persons with lung cancer have pain or other symptoms prior to diagnosis</td>
<td></td>
<td>32</td>
<td>22</td>
<td>.004</td>
</tr>
<tr>
<td>There is not much you can do to lower your chance of getting lung cancer</td>
<td></td>
<td>14</td>
<td>19</td>
<td>.3</td>
</tr>
<tr>
<td>Lung cancer is caused by behavior or lifestyle</td>
<td></td>
<td>85</td>
<td>73</td>
<td>.013</td>
</tr>
<tr>
<td>Getting checked regularly for lung cancer increases the chances of finding it</td>
<td></td>
<td>90</td>
<td>81</td>
<td>.06</td>
</tr>
<tr>
<td>Compared with the average person, would you say that you are</td>
<td></td>
<td>28</td>
<td>25</td>
<td>.20</td>
</tr>
<tr>
<td>About as likely</td>
<td></td>
<td>60</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Less likely</td>
<td></td>
<td>12</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>More likely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, how many people who develop lung cancer survive for 5 years?</td>
<td></td>
<td>16</td>
<td>26</td>
<td>.05</td>
</tr>
<tr>
<td>&lt;25%</td>
<td></td>
<td>30</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>About 25%</td>
<td></td>
<td>42</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>About 50%</td>
<td></td>
<td>9</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>About 75%</td>
<td></td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Nearly all</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HINTS indicates Health Information National Trends Survey.

Lathan et al., Cancer, 2010
Perceptions Regarding Lung Cancer

Racial and Ethnic Differences in Beliefs About Lung Cancer Care

Sririsha Jonnalagadda, MD; Jenny J. Lin, MD; Judith E. Nelson, MD, JD, FCCP; Charles A. Powell, MD; John Salazar-Schicchi, MD, Andrew R. Berman, MD, FCCP; Steven M. Keller, MD, FCCP; Cardinale B. Smith, MD, MSCR; Linda Lurslurchachai, MPH; Ethan A. Hahn, MD, MPH; Howard Leventhal, PhD; and Juan P. Wisnivesky, MD, DrPH

- 335 patients surveyed regarding beliefs about lung cancer treatment
- Median time for enrollment was within 3 months of diagnosis
- Major areas of difference included attitudes towards surgery, fatalistic beliefs, advanced directives and hospice
- Similarities regarding open discussion about prognosis
Risk Factors for NSCLC

- Smoking (85% of cases)
- Occupational carcinogens
  - Asbestos
  - Radon
  - Nickel
- Nutrition/Diet
- Genetic factors
- 2nd Hand Smoke (~5%)
Proactive Tobacco Cessation Outreach to Smokers of Low Socioeconomic Status
A Randomized Clinical Trial

Jennifer S. Haas, MD, MSc; Jeffrey A. Linder, MD, MPH; Elyse R. Park, PhD, MPH; Irina Gonzalez, MD, TTS; Nancy A. Rigotti, MD; Elissa V. Klinger, ScM; Emily Z. Kontos, ScD; Alan M. Zaslavsky, PhD; Phyllis Brawarsky, MPH; Lucas X. Marinacci, BA; Stella St Hubert, AB; Eric W. Fleegler, MD, MPH; David R. Williams, PhD, MPH

Smoking Cessation Among African American and White Smokers in the Veterans Affairs Health Care System

Diana J. Burgess, PhD, Michelle van Ryn, PhD, MPH, Siomak Noorbaloochi, PhD, Barbara Clothier, MS, MA, Brent C. Taylor, PhD, Scott Sherman, MD, MPH, Anne M. Joseph, MD, MPH, and Steven S. Fu, MD, MSCE

Targeting cessation: Understanding barriers and motivations to quitting among urban adult daily tobacco smokers

Lisa Rosenthal a,b, Amy Carroll-Scott a, Valerie A. Eamshaw a, Naa Sackey a, Stephanie S. O’Malley b, Alycia Santilli a, Jeannette R. Ickovics a

Smoking Behavior and Lung Cancer in a Biracial Cohort
The Atherosclerosis Risk in Communities Study

Anna E. Prizment, PhD, Hiroshi Yatsuya, MD, PhD, Pamela L. Lutsey, PhD, Jay H. Lubin, PhD, Mark Woodward, PhD, Aaron R. Folsom, MD, Rachel R. Huxley, DPhil
Menthol Cigarettes: Myth or Fact?

- Preferred among 83% of AA and 23% of caucasians
- Southern Community Cohort study
- Prospective study
- 440 incident lung cancers and 2213 matched controls
- Menthol does not increase risk of lung cancer (studies are varied)
- Quitting rates similar for menthol or non-menthol

Blot et al., JNCI, 2011

Table 2. Lung cancer incidence in relation to menthol and non-menthol cigarette smoking*

<table>
<thead>
<tr>
<th>Baseline smoking status, type of cigarette, cpd†</th>
<th>OR (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoker</td>
<td>1.0 (Referent)</td>
</tr>
<tr>
<td>Current, nonmenthol, ≥20 cpd</td>
<td>21.1 (12.2 to 36.5)</td>
</tr>
<tr>
<td>Current, nonmenthol, 10–19 cpd</td>
<td>12.9 (7.3 to 23.0)</td>
</tr>
<tr>
<td>Current, nonmenthol, &lt;10 cpd</td>
<td>10.3 (5.5 to 19.3)</td>
</tr>
<tr>
<td>Current, menthol, ≥20 cpd</td>
<td>12.2 (7.2 to 20.8)</td>
</tr>
<tr>
<td>Current, menthol, 10–19 cpd</td>
<td>8.7 (5.2 to 14.7)</td>
</tr>
<tr>
<td>Current, menthol, &lt;10 cpd</td>
<td>5.0 (2.9 to 8.6)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>4.4 (2.8 to 6.9)</td>
</tr>
</tbody>
</table>

Table 3. Lung cancer mortality in relation to menthol and non-menthol cigarette smoking*

<table>
<thead>
<tr>
<th>Baseline smoking status, type of cigarette, cpd†</th>
<th>HR (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoker</td>
<td>1.0 (Referent)</td>
</tr>
<tr>
<td>Current, nonmenthol, ≥20 cpd</td>
<td>16.1 (9.2 to 28.3)</td>
</tr>
<tr>
<td>Current, nonmenthol, 10–19 cpd</td>
<td>14.2 (7.8 to 25.8)</td>
</tr>
<tr>
<td>Current, nonmenthol, &lt;10 cpd</td>
<td>9.9 (5.0 to 19.6)</td>
</tr>
<tr>
<td>Current, menthol, ≥20 cpd</td>
<td>13.9 (7.9 to 24.3)</td>
</tr>
<tr>
<td>Current, menthol, 10–19 cpd</td>
<td>8.3 (4.6 to 14.9)</td>
</tr>
<tr>
<td>Current, menthol, &lt;10 cpd</td>
<td>4.6 (2.4 to 8.7)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>4.7 (2.8 to 8.0)</td>
</tr>
</tbody>
</table>
Smoking is common among patients with cancer (U.S. Studies only)

<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>% Current Smokers</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>10-33%</td>
<td>Moreira, 2014 Kenfield, 2011</td>
</tr>
<tr>
<td>Breast</td>
<td>7-10%</td>
<td>Pierce, 2013 Chang, 1999</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11-20%</td>
<td>Sharma, 2013 Phipps, 2011</td>
</tr>
<tr>
<td>Lung</td>
<td>20-25%</td>
<td>Mason, 2009 Williams, 2006</td>
</tr>
<tr>
<td>Heme Stem Cell Transplant</td>
<td>15%</td>
<td>Ehlers, 2011</td>
</tr>
<tr>
<td>Renal</td>
<td>15%</td>
<td>Parker, 2008</td>
</tr>
<tr>
<td>Cervical</td>
<td>50%</td>
<td>Coker, 2009 Wright, 2005</td>
</tr>
<tr>
<td>Ovarian</td>
<td>17%</td>
<td>Nagle, 2006</td>
</tr>
</tbody>
</table>
Major Messages NNCN Guidelines 2015

- There are health benefits of smoking cessation, even after a cancer diagnosis
  - Any stage and prognosis
  - Smoking affects treatment toxicity, outcomes, disease recurrence and secondary cancers

- There are established methods for helping a patient quit

- Smoking and nicotine addiction is a chronic and relapsing disorder
  - Patients with cancer typically are more nicotine dependent and have an unsuccessful history of quitting attempts

- Treatment plans should include evidence-based pharmacotherapy and behavior therapy (counseling), close follow-up, and adequate documentation in the medical record
  - Guidelines are specific to patients with cancer and cancer survivors
Genetic/Enviromental risk factors

- Cytochrome P450 (CYP1A1): Increased risk for lung cancer among Latinos (Aldrich, et al., 2009)
- Base excision repair
- DNA repair and cell cycle control (AA women) (Zheng, IJC 2010)
- D2 Dopamine receptor (Wu X, Spitz, M, 2000)
- MET (Krishnaswamy, Clin Can Res, 2009)
- P53 (Jin, Spitz, M 1995)
- KRAS (Hunt et al., 2002)
- Vitamin D (Grant et al., 2012)
Nicotine and Cancer

Improgo et al. *Oncogene*, 2010
Nicotinic receptor and lung cancer risk in AA (“fine mapping”)

- Northern California Lung Cancer Study
- 448 cases and 611 controls (77.8% African ancestry)
- Multiple lung cancer risk loci identified
  - rs17486278 (1st intron of CHRNA5) increased risk (OR 1.54) despite controlling for smoking behavior. Lack of linkage to rs16969968
  - rs 7178270 (between 1st and 2nd introns of CHRN4B) decreased risk in women but not men (OR 0.62)
  - Rs7168796 and rs7164594 in the LOC123688 gene (GG and AA reduced lung cancer risk)
  - Four SNP haplotype (rs11637635 C, rs17408276 T, rs 16969968 G (CHRNA5) rs5787776 G (CHRNA3) increased lung cancer risk
  - Rs564585 and rs8029939 alter microRNA binding

Hansen et al., Hum Mol Genet, 2010
Snapshot of Genetic Environmental Studies

San Francisco Bay Area
Latinos 113/299 AA 255/280
Base Excision Repair SNPs
XRCC1 Arg 399Gln increased risk in Latinos NOT African Americans
Chang et al., Carcinogenesis, 2009)

San Francisco Bay Area
Latinos/AA
422 cases/894 controls
Prolonged Tar and asphalt Exposure associated with increased Lung cancer risk Mclean et al., Am Jour Indus med, 2011)

Evans County Heart Study
Charleston Heart Study
5,363 individuals (1960-00)
CS strong risk factor among Caucasians but not AA
Stage Determines Outcome

Lung Cancer Diagnosis and Survival By Stage, 2004-2010

- Localized (confined to primary site)
- Regional (spread to regional lymph nodes)
- Distant (cancer has metastasized)
- Unstaged tumors not shown

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15%</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>22%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57%</td>
<td></td>
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</tbody>
</table>

5-Year Relative Survival:
- 54%
- 27%
- 4%
Late Presentation of Disease Contributes to Mortality

Age and Stage at Diagnosis

- Mortality rates from tobacco related malignancies are 2-4 times more likely to have lung cancer even when adjusting for cigarette use.
- AA patients with lung cancer more among AAs are 13% higher than Caucasians.
- AA men likely to be male and receive chemo/rads while white patients more likely to undergo surgery. AA more likely to present with later stage with the exception of Medicaid (Efird, 2014).
- AA tend to be younger at time of diagnosis (Robbins, JNCI, 2014).
NLST

- Randomized CXR versus low-dose helical CT scan
- Initially screening followed by annual for two years
- 53,454 participants
- Ages 55-74
- Heavy smoker or former smoker (30 pack years)
- Asymptomatic
- No prior cancer
- Powered to detect 20% reduction in mortality
NLST (2002-2009)

- Initial screening 39% positive rate in low-dose CT and 16.0% in CXR
- 96.4% (CT) and 94.5% (CXR) false positive rate
- 1600 (CT) and 941 (CXR) lung cancers
- 20% reduction in lung cancer related mortality
- 6.7% reduction in all cause mortality
- 91% Caucasian, 4.5% AA, 1.8% Latino

NEJM, 2011
Screening in AA and Latinos

- 108 high risk individuals (40% non-minorities, 37% AA, 32% Hispanics); urban hospital
- 55-74 years of age, 10 pk years
- 82% willing to undergo screening if at no financial cost
- Intention to undergo screening decreased by 50% if cost associated
- Only 15% of Hispanics willing to be screened if there is cost
- Among AA and Hispanics more misunderstanding regarding lung cancer causes and risk, more fatalistic

Jonnalagadda et al, Lung Cancer, 2012
Implementing Lung Cancer Screening in the Era of CMS Coverage

Lung Cancer Screening Program Overview

At the OSUCCC – James we strongly believe that the early detection of lung cancer when it is most curable is essential to increasing the number of survivors and decreasing the number of deaths from lung cancer. The National Lung Screening Trial showed that computed tomography (CT) screening significantly reduces lung cancer deaths in people over the age of 55 who have a smoking history.

However, it is very important that these scans be done correctly to minimize radiation exposure and maximize benefit. Since the scans are very sensitive and thus need to be interpreted by a multidisciplinary team of physicians from a variety of specialties, including pulmonary medicine, medical oncology, surgery and pathology. In addition to radiology, we have assembled these experts into a formal lung screening program in order to maximize the benefit to your patient from this test. In addition, we are conducting research to develop blood tests for lung cancer, and your patient will have the opportunity to participate in this research as part of this program.

- Shared Decision Making
- Lung Rads for standardization of reporting
- Registry
- Management of incidental findings
- Rapid Diagnostics
- Smoking Cessation
Impact of Screening

2013

2015
Biomarkers for Early Detection (Future)

- NCODE array
- ~500 human miRNA in triplicate

Serum
PBMC
Red blood cells

Exosomes in serum

Molecular beacon containing tethered cationic lipoplex nanoparticles (tCLN)

miR-21 containing exosomes

TIRF: total internal reflection fluorescence

MiR-21 detected in lung cancer patient serum

TIRF: total internal reflection fluorescence
Treatment
Health Disparities in Staging and Outcomes

- Hispanics and non-whites less likely to undergo PET as part of staging (Gould, et al. JTO, 2011) CanCORS

- Among Medicare patients with stage I and II lung cancer, AA were 66% less likely to receive timely and appropriate care and 34% less likely to receive timely treatment for advanced disease. (Shugarman, 2009)

- Females have improved surgical outcome (Lapar et al., Ann Thorac Surg, 2011)

- Decreased surgical complications among AAs, Hispanics and Asians (Lapar et al., Ann Thorac Surg, 2011)
Disparities in surgery for early stage NSCLC

SEER Database 62,514
Refusal
1.4% Caucasians
2.0% AA
2.8% other

Chemotherapeutic Response in AA does not differ

Stage IIIB/IV NSCLC
- gemcitabine/carboplatin
- gemcitabine/paclitaxel
- paclitaxel/carboplatin

Outcome Toxicity

972 Caucasian and 138 AA
Median survival: 8.3 mo in Caucasians and 9.1 mo in AA
Time to progression: 4.6 mo. Caucasians 4.3 mo. AA
No difference in non-hematological toxicities

Obasaju et al., *Journal of Thoracic Oncology*, 2010
Small cell lung cancer in AA

- Previous data to suggest that AA with extensive small cell less likely to receive chemotherapy (Earle et al, JCO, 2002)

- Evaluation of 928 non-AA and 67 AA undergoing chemotherapy for extensive stage small cell lung cancer in the setting of Phase II or III clinical trials in CALGB

- Median survival 11.5 mo. AA and 9.9 in non-AA

Blackstock et al., JCO, 2006
Does Equal Access Make a Difference?

Lung Cancer Survival among Black and White Patients in an Equal Access Health System

Li Zheng¹, Lindsey Enewold¹, Shelia H. Zahm², Craig D. Shriver¹,³,⁴, Jing Zhou¹, Aizen Marrogi⁵, Katherine A. McGlynn², and Kangmin Zhu¹,⁴

Cancer Epidemiology, Biomarkers and Prevention, 2012
LCMC Distribution of Mutations

Mutation found in 54% (280/516) of tumors completely tested (CI 50-59%)
Lung Cancer Mutation Consortium
Lung Cancer: The Present and Future

Comprehensive genomic characterization of squamous cell lung cancers

The Cancer Genome Atlas Research Network®

African Americans?
Latinos?
EGFR : A good target for lung cancer

- High level of receptor expression compared with healthy tissue.
- EGFR - Key role in tumor cell growth & function.
- EGFR inhibition can inhibit downstream activity.
- EGFR inhibitors have no severe toxicity.
- Exon 19 in frame deletion and exon 21 point mutations most common
- Women, nonsmokers, Asian
Drugs Available

- Gefitinib
  Highly selective, potent & reversible EGFR Tyrosine Kinase Inhibitor
- Erlotinib
- Cetuximab – Monoclonal Anti EGFR antibody

- H 447
  Bispecific Anti EGFR antibody linked to Anti CD 64
- MDX 210
EGFR inhibitor as first line therapy

**Chemotherapy**  
N=96 (Median PFS = 166 days)

**Gefitinib**  
N=98 (Median PFS = 317 days)

**Logrank test**  
P < 0.001 ***

### Progression-Free Survival (%)

<table>
<thead>
<tr>
<th>Days after Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Gefitinib</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate</td>
<td>73.7%</td>
<td>30.7%</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>9.6%</td>
<td>14.0%</td>
</tr>
</tbody>
</table>

NEJM 2010;362:2380
## Differences in EGFR mutation

<table>
<thead>
<tr>
<th>Study</th>
<th>Caucasians</th>
<th>African Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al. <em>Clin Can Res.</em>, 2005 (n=219)</td>
<td>14.1%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Leidner et al., J Thorac Oncol., 2009 (n=155)</td>
<td>17%</td>
<td>2% ***</td>
</tr>
<tr>
<td>Cote et al., J Thorac Oncol., 2011 (n=144)</td>
<td>15.6%</td>
<td>11.9%</td>
</tr>
</tbody>
</table>
| Harada et al, Oncogene, 2010              |            | Rare insertional 2 mutations in exon 20 (N771GY and A-767-V769 dup) unresponsive to Erlotinib but sensitive to other TKI

***No Difference in Kras***
Identification of the transforming EML4–ALK fusion gene in non-small-cell lung cancer

Manabu Soda¹,², Young Lim Choi¹, Munehiro Enomoto¹,², Shuji Takada¹, Yoshihiro Yamashita¹, Shunpei Ishikawa⁵, Shin-ichiro Fujiwara¹, Hideki Watanabe¹, Kentaro Kurashina¹, Hisashi Hatanaka¹, Masashi Bando², Shoji Ohno², Yuichi Ishikawa⁶, Hiroyuki Aburatani⁵,⁷, Toshio Niki³, Yasunori Sohara⁴, Yukihiro Sugiyama² & Hiroyuki Mano¹,⁷

- Echinoderm microtubule-associated protein-like 4 (EML4) becomes fused with the anaplastic lymphoma kinase (ALK)
  - Inversion within chromosome 2p
- First identified in 2007 from a resected lung adenocarcinoma specimen
- Clinical evaluation
  - Young
  - Never/light smokers
  - Male predominance
  - Adenocarcinoma histology
ALK inhibition in Lung Cancer (Crizotinib)

- 82/1500 identified with mutation
- 57% response
- Estimated 6 month PFS 72% (median not reached)
- OS not reached
- Incidence in AA?

NEJM 2010;363:1693
Somatic mutation spectrum of non-small cell lung cancer in African Americans: a pooled analysis

Luiz H. Araujo, MD, MSc¹,*, Philip E. Lammers, MD, MSc²,*, Velmalia Matthews-Smith, MD³, Rosana Eisenberg, MD⁴, Adriana Gonzalez, MD⁵, Ann G. Schwartz, PhD, MPH⁶, Cynthia Timmers, PhD¹, Konstantin Shilo, MD¹, Weiqiang Zhao, MD, PhD¹, Thanemozhi G. Natarajan, PhD⁷, Jianying Zhang, PhD⁸, Ayse Selen Yilmaz, MSc¹,⁸,⁹, Tom Liu, PhD¹, Kevin Coombes, PhD¹,⁸, and David P. Carbone, MD, PhD¹

Table 1 – Baseline characteristics (N=260)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range)</td>
<td>60 (35-85)</td>
</tr>
<tr>
<td>Gender N (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>162 (62.3)</td>
</tr>
<tr>
<td>Female</td>
<td>96 (36.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Smoking Status N (%)</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>165 (63.5)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>60 (23.1)</td>
</tr>
<tr>
<td>Never smoker</td>
<td>25 (9.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (3.8)</td>
</tr>
<tr>
<td>Histology N (%)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>137 (52.7)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>81 (31.2)</td>
</tr>
<tr>
<td>NSCLC, NOS</td>
<td>27 (10.4)</td>
</tr>
<tr>
<td>Others</td>
<td>15 (5.7)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>114 (43.8)</td>
</tr>
<tr>
<td>II</td>
<td>33 (12.7)</td>
</tr>
<tr>
<td>III</td>
<td>41 (15.8)</td>
</tr>
<tr>
<td>IV</td>
<td>62 (23.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (3.8)</td>
</tr>
</tbody>
</table>

Abbreviations: NSCLC, Non-small cell lung cancer; NOS, not otherwise specified.
Lung Cancer Survivorship

- **Financial Toxicity:** Up to 40% of cancer care patients worry about cost of care and 1/3 report cancer related financial problems (higher among minorities).

- Trend towards higher proportion of AA and Hispanic survivors report economic hardship one year following lung cancer treatment (*Pisu et al, 2014*).

Case Presentation

- 56 year old African American male presents for discussion regarding new diagnosis of advanced stage NSCLC
- PMHx: DM, HTN
- SocHx 40 pack year smoker, no drugs no ETOH
- FamHx: positive for prostate cancer, HTN
- Examination: decreased breath sounds bilaterally, otherwise unremarkable
- He has been reading about genetic testing of tumors and is enquiring about his prognosis and best treatment options

How do you counsel him?
Conclusions

- In the U.S. AAs have higher tobacco related malignancy incidence and mortality
- Intention to undergo screening reduces significantly if cost is associated
- Histological and outcome differences between AA and Hispanics
- Genetic/environmental explanations likely to be more successful in encouraging treatment and clinical trial enrollment
- Similar responses to standard chemotherapy between AA and Caucasians
- Novel EGFR mutations in AA
Addressing Disparities in Lung Cancer Care

- Early Detection
- Cultural Competency Awareness Outreach
- Survivorship
- Clinical Trials Mutational Analysis
- Smoking Cessation
- Equal Access Rapid Diagnostics Navigation

The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute