Global incidence and mortality

Global Cancer Incidence and Mortality, 1990-2016

Incidence
- Lip and oral cavity cancer
- Nasopharynx cancer
- Other pharynx cancer
- Esophageal cancer
- Stomach cancer
- Colon and rectum cancer
- Liver cancer
- Gallbladder and biliary tract cancer
- Pancreas cancer
- Larynx cancer
- Trachea, bronchus, and lung cancer
- Melanoma skin melanoma
- Squamous cell carcinoma
- Blast cell leukemia
- Kidney cancer
- Bladder cancer
- Bone and soft tissue sarcoma
- Thyroid cancer

Mortality
- Lip and oral cavity cancer
- Nasopharynx cancer
- Other pharynx cancer
- Esophageal cancer
- Stomach cancer
- Colon and rectum cancer
- Liver cancer
- Gallbladder and biliary tract cancer
- Pancreas cancer
- Larynx cancer
- Trachea, bronchus, and lung cancer
- Bone and soft tissue sarcoma
- Thyroid cancer

Graphs showing trends in incidence and mortality over age and gender. Notably, Lung Cancer is highlighted as a major concern.
Cancer Statistics, 2018

US Lung Cancer Statistics, 2018

- 234,030 estimated new cases (lung and bronchus)
- 154,050 estimated deaths
- leading cause of cancer deaths
  - greater than breast+prostate+colon
  - death rate per 100,000 decreasing (90.56 in 1990; 67.45 in 2006)
    - Incidence declining in men since mid-1980’s, women since mid-2000’s
- 18% five year survival
  - 5% in 1950’s, 13% in 1970’s
  - 26% of all male cancer deaths, 25% of all female cancer deaths

Risk factors

Risk Factors

- Tobacco, tobacco, tobacco (85% lung ca.)
  - Including passive smoking
  - Prior aerodigestive malignancy
  - COPD
- Other exposures
  - Asbestos, radon, polycyclic aromatic hydrocarbons, chromium, nickel, inorganic arsenic – mining, ship building, oil refining
- Genetic predisposition
  - Familial lung cancer – Germline mutations - EGFR T790M
    - Bell et al., Nat Gen 2005;37:1315
  - 15q24-25.1 – nicotinic acetylcholine receptor subunits CHRNA3 and CHRNA5, OR=1.3, attributable risk –14%
  - CH3NA3/5 is also susceptibility locus for COPD
    - Pillai et al. PLoS Genet 2009;5:1
Pathology: NSCLC

- Adenocarcinoma, inc bronchoalveolar — 40%
- Squamous cell carcinoma — 20%
- Large cell carcinoma — 15%
- Others (carcinoid, etc.)
Lung carcinogenesis

The Continuum of Lung Carcinogenesis
Opportunities for Intervention

Normal → Hyper/Metaplasia → Dysplasia → Early-Late Cancer

Prevention

Early Detection

Treatment
Treatment Strategies for Lung Cancer

- Treatment based on stage:
  - Early stage (Stage I) – surgery
  - Early stage (Stage II, IIIA resected)-surgery + adjuvant chemo
  - Regional spread (IIIA/IIIB) – combined modality (chemoradiation; +/- surgery for IIIA)
  - Metastatic (IIIB “wet”/IV)– chemotherapy, radiation as needed for local control, occasional resection of isolated metastases

- Small cell lung cancer: chemotherapy (+thoracic radiation for limited stage; prophylactic cranial radiation to prevent brain mets)
Treatment options

Treatment Options for Metastatic NSCLC

- Chemotherapy
  - Platinum doublets, iv
  - Adjuvant, metastatic disease
  - Still a mainstay of treatment
- Targeted therapy
  - For minority of patients with targetable mutations
  - Oral therapies, better tolerance
  - Extended survival
- Immunotherapy
  - Now a definitive role, frontline and second line
Personalizing Therapy for NSCLC

Genetic Abnormalities in Lung Adenocarcinoma

-Berge and Doebele, Sem Oncol 2014;41:110
EGFR as a Target for NSCLC
Standard of Care in 2015

- Epidermal growth factor receptor (EGFR) inhibition in advanced NSCLC
  - 10% response rate in advanced disease, 30% prolonged stabilization
  - Survival advantage (erlotinib)
  - Mutually exclusive with K-ras
  - Most benefit for non-smoking related NSCLC, with EGFR mutations (females, adenocarcinomas, Asian)
  - Mechanisms of secondary resistance to EGFR inhibitors being identified (T790M mutation-50%, Met amplification-10-20%, others), new drugs
- Erlotinib approved as single agent for 1st, 2nd and 3rd line treatment of NSCLC
  - Also for maintenance after 1st line non-progression after chemo
  - Afatinib, gefitinib also approved
EML4-ALK Fusion Gene as a Target for NSCLC

- Identified in 2007
- ~5% NSCLC, mainly never smokers
- Striking response to inhibitor – crizotinib- 57% RR, 33% stable disease (FDA approved)
  - Kwak EL et al. NEJM 2010;363:1693
- 2nd line agent approved (ceritinib), 56% RR
  - Shaw AT, et al. NEJM 2014;370:1189
- Multiple mechanisms of resistance

Shaw AT et al., JCO 2009;27:4247
ROS1 Rearrangements

ROS1 Rearrangements as a Target

- Tyrosine kinase (insulin receptor family)
- 1.7% of NSLC have rearrangements
- Multiple different partners
- crizotinib – RR=72%, median duration 17.6 mths
  - Shaw AT et al., NEJM 2014;371:1963
New Approaches - Immunotherapy

• PD-1
  – T-cell co-inhibitory receptor, regulates T-cell activation
  – Main role: to limit activity of T cells in peripheral tissues during inflammatory response to infection and to limit autoimmunity
  – ligands PD-L1 (frequently expressed on tumors) and PD-L2
  – Blockade of PD-L1/PD-1 interaction potentiates immune response (to tumor)

Pardoll D Nat Rev Cancer 2012;12:252
Immunotherapy

New Approaches - Immunotherapy

- Anti-PD-1 antibodies approved for 2\textsuperscript{nd} line NSCLC; nivolumab and pembrolizumab (PD-L1+)
  - \(\sim\)20\% response rate (vs. 10\% docetaxel)
  - \(\sim\)3 month improved overall survival nivolumab c/w docetaxel
  - Long term responses (median duration 12.5 mths with pembrol)

Squamous, nivolumab:


Second line immunotherapy

Second line immunotherapy treatment

- Anti-PD-1 antibodies approved; nivolumab and pembrolizumab (PD-L1+)
  - ~20% response rate (vs. 10% docetaxel)
  - ~3 month improved overall survival nivolumab c/w docetaxel
  - Long term responses (median duration 12.5 mths with pembro)

- Anti-PD-L1 antibody: atezolizumab - similar efficacy


Approaches to reducing cancer morbidity and mortality

- Prevention (primary, secondary, tertiary)
- Early detection

- Better therapeutics
Smoking Cessation and Lung Cancer

Effect of Smoking Cessation on Lung Cancer Death
Lung Health Study, 14.5 yr F/U

Anthonisen et al., Ann Intern Med 142:233, 2005
Lung carcinogenesis

The Continuum of Lung Carcinogenesis
Opportunities for Intervention

Normal $\rightarrow$ Hyper/Metaplasia $\rightarrow$ **Dysplasia** $\rightarrow$ Early-Late Cancer

- Prevention
- Early Detection
- Treatment
Cancer Chemoprevention

The use of natural or synthetic agents to suppress or reverse carcinogenesis

- Regress existing neoplastic lesions (treat intraepithelial neoplasia)
- Prevent development of new neoplastic lesions (preneoplastic and cancer)
- Suppress recurrence of neoplastic lesions
Lung Cancer Prevention

**Rationale for Lung Cancer Prevention**

- Metastatic cancer is rarely curable
  - US lung cancer 5 yr survival is $\sim$15% (5% 1950’s, 13% 1970’s)

- Cancer is preventable
  - P1, STAR breast cancer prevention trials with tamoxifen and raloxifene
    - *Fisher B et al., JNCI 1998;190:1371; Vogel, VG et al., JAMA 2006;295:2727*
  - Multiple animal studies with multiple agents

- Long preclinical phase with increasing histologic and molecular abnormalities, identifiable populations at risk
Efficacy: How Do We Identify New Agents?

- **Knowledge of mechanism**
  - Example: HPV vaccine and cervical cancer
  - Need: understanding molecular pathogenesis

- **Preclinical (in vitro and animal models)**
  - Example: NSAID treated carcinogenesis and transgenic models
  - Need: models reflective of complexity of human disease

- **Observational epidemiology (cohort and case-control studies)**
  - Example: NSAIDs and colon cancer incidence/mortality

- **Secondary endpoints from clinical trials (including other diseases)**
  - Example: Tamoxifen/raloxifene and breast cancer
Clinical agents

Clinical Agent Development – What are the major issues?

- Targets/agent selection – correctly match target/agent to right process/person (Precision Medicine)
  - Different pathogenesis/progenitor cell lineages → different intervention?
  - Temporal considerations – accumulating molecular abnormalities over time may require different strategies to be delivered at different time points

- Cohort selection
  - Squamous (central) cancers – bronchial dysplasia?
  - Adenocarcinoma (peripheral) cancers – lung nodules?
  - Other histologies - ???

- Risk-benefit balance
  - Efficacy vs. tolerability or major adverse side effects

- Endpoints – cancer for phase III, intermediate endpoints (preliminary efficacy) for phase II

- Clinical trial designs
Targeting Inflammation for Lung Cancer Prevention: Rationale

• Animal data showing role for steroids in cancer prevention
  – 1970’s – skin
  – Early 1990’s – lung (oral steroids)
  – Late 1990’s – lung (inhaled steroids)

• Epidemiology/Human data –
  – Mainly negative (but studies of short exposure duration)
  – VA cohort with COPD (n=10,474) – HR 0.39 (95% CI, 0.16-0.96)
  • Parimon T et al., AJRCCM 175:712, 2007
Budesonide and Lung Tumorigenesis

**Effect of Budesonide on Mouse Lung Tumorigenesis**

-82% decrease in tumors

-Shift from adenoma to carcinoma

*Pereira et al., Carcinogenesis 2002*
Bronchial Dysplasia

Premalignant Squamous Lesions
Bronchial Dysplasia – precursor and risk marker

Invasive SCC variants: Keratinizing, Non-keratinizing, Basaloid, Papillary

Images showing various stages of dysplasia with corresponding HS scores.
Squamous cell carcinoma precursor

Squamous Cell Carcinoma Precursor: Bronchial Dysplasia

- Progression to cancer based on bronchoscopic dx, median 2-3 yr f/u (Bota et al., Am J Respir Crit Care Med 2001:164;1688; Venmans et al., Chest 2000:117;1572; Breuer et al. Clin Cancer Res 2005:11;537)
  - Metaplasia: 37-42% regress, 2-9% CIS/cancer (at 4-59 mths)
  - Mild/moderate dysplasia: 37-64% regress, 9% CIS/cancer (at 7-57 mths)
  - Severe dysplasia: 41-52% regress, 32% CIS/cancer (1-32 mths)
  - Carcinoma in situ: 56% progress at site (44% also had severe dysplasia or CIS elsewhere)

- 164 pts. with low or high-grade lesions (Van Boerdonk et al., Am J Respir Crit Care Med 2015;192:1483)
  - 33.5% developed invasive cancer, median 16.5 mths
  - 41% cancers developed from abnormal site, 59% from other sites (central or peripheral)
  - High grade lesions assoc with cancer; COPD and prior hx lung ca assoc with OS

- Bronchial dysplasia both precursor and risk marker for abnormal field
Phase IIb Trial

DCP Phase IIb Trial of Inhaled Budesonide in Bronchial Dysplasia

112 smokers with dysplasia

Bronch, Helical CT

Budesonide vs. Placebo x 6mths

Bronch, Spiral CT

# Screened (sputum): 1040
Cancers detected: 13

1º Endpoint: bronchial dysplasia (#sites/grade)
2º Endpoints: multiple biomarkers
Inhaled Budesonide

Phase IIb Trial of Inhaled Budesonide in Bronchial Dysplasia

- Bronchial dysplasia – no effect of 6 mth Rx
- CT-detected lung nodules - 27% vs. 12% resolved (p=0.024)

Lam et al., Clin Cancer Res 2004;10:6502
Budesonide Trial

Phase IIb Budesonide Trial in CT-Detected Lung Nodules

202 participants with persistent LD-CT-detected peripheral nodules

Randomize

inhaled budesonide vs. placebo x 1 year

repeat LD-CT

Primary endpoint: shrinkage of lung nodules

Veronesi et al., Cancer Prev Res 2011;4:34-42
Chemoprevention Trial

Phase IIb Budesonide Chemoprevention Trial
Lesion Specific Analysis

12 months

5-yr f/u, non-solid

p=.029

-Overall response negative, but trend toward regression in non-solid lesions (putative precursors of adenocarcinoma)

Veronesi et al., Cancer Prev Res 2011;4:34-42
Veronesi et al., Ann Oncol 2015;26:1025-30
Atypical Adenomatous Hyperplasia

Adenocarcinoma Precursor: Atypical Adenomatous Hyperplasia

- Natural history not well understood
- Localized ground glass opacities on CT:
  - AAH 25%; bronchoalveolar ca 50%; invasive adenocarcinoma 10%; fibrosis 15% (Nakajima et al., J Comput Assist Tomogr 2002;26:323)
  - AAH 63%; bronchoalveolar ca 34%; scar 3% (Ohtsuka et al., Eur J Cardio-Thor Surg 2006;30:160)
Non-solid nodules

Non-solid nodules – Natural History

- Prospective trial, 795 patients with 1229 subsolid nodules (GGNs, ≤3cm, solid component ≤5 mm)
  - f/u 4.3±2.5 years
  - 1046 pure GGN → 5.4% became part solid
  - 81 heterogeneous GGN → 19.8% became part solid
  - Resected nodules (in 80 patients)
    - 35/997 pure GGNs (9 MIA, 21 AIS, 5 AAH)
    - 7/78 heterogeneous GGNs (5 MIA, 2 AIS)
    - 49/174 part solid GGNs (12 invasive, 26 MIA, 10 AIS, 1 AAH)

- 1% of all nodules became invasive cancer (all were part solid)
- 3.3% became MIA, 2.7% AIS, 0.5% AAH

Kakinuma et al., J Thor Oncol 2018;11:1012
CT-detected Lung Nodule

Evolution of CT-detected Lung Nodule

4-1-04

7-14-04

8-19-10

7-25-11

Dx:
Invasive adenocarcinoma (stage I)
Adjacent AAH
Non-calcified nodules

Non-calcified nodules (NCN)
Risk of Lung Cancer in the NLST

<table>
<thead>
<tr>
<th></th>
<th>0-23 Months HR (95% CI)</th>
<th>24-59 Months HR (95% CI)</th>
<th>60-84 Months HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 10+ mm NCN (vs. only 4-9 mm NCNs)</td>
<td>12.8 (9.5-17.2)</td>
<td>4.7 (2.9-7.5)</td>
<td>N.S.</td>
</tr>
<tr>
<td>≥1 NCN w/ Spiculated or Poorly Defined Margins (vs. only NCNs with smooth margins)</td>
<td>4.1 (3.0-5.5)</td>
<td>2.3 (1.5-3.5)</td>
<td>N.S.</td>
</tr>
<tr>
<td>≥1 Persistent NCN (vs. non-persistent NCNs)</td>
<td>N/A</td>
<td>4.8 (2.8-8.3)</td>
<td>N.S.</td>
</tr>
<tr>
<td>≥1 NCN w/ Ground Glass Attenuation (vs. soft tissue attenuation)</td>
<td>0.3 (0.2-0.4)</td>
<td>N.S.</td>
<td>3.1 (1.4-6.6)</td>
</tr>
</tbody>
</table>

Interpretation:
Increased long-term risk of ground glass nodules suggests some are lung cancer precursors

Mutational spectrum

Mutational Spectrum of Adenocarcinoma Precursors

- Targeted next-generation sequencing
- 6 patients with AAH (5 smoking history), 5 AIS, 5 MIA
- Spectrum differs
  - AAH – only p53 and EGFR (1 pt.) or Kras (1 pt) shared with tumor
  - AAH: 4/6 BRAF
  - DNA repair abn in most
  - Heterogeneity in preinvasive lesions

Izumchenko E et al., Nature Com 2015
Aspirin and Mortality

Effect of Aspirin on Lung Cancer Mortality
- Rothwell et al., Lancet 2011;377:31

-individual patient data from trials of ASA vs. none

-lung:

<table>
<thead>
<tr>
<th>f/u</th>
<th>0-10 yrs</th>
<th>0-20 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>0.68</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>(0.50-0.92, p=0.01)</td>
<td>(0.58-0.89, p=0.002)</td>
</tr>
</tbody>
</table>

-adenocarcinoma only

-benefit only after 5 yrs
A Randomized Phase II Trial of Low Dose Aspirin versus Placebo in High-Risk Individuals with CT Screen Detected Subsolid Lung Nodules

PIs: Giulia Veronesi, MD and Bernardo Bonanni, MD; IEO

128 asymptomatic current and former smokers
>20 pack yr
Age >50

LD-CT scan
Persistent non-solid or part-solid nodules
ASA 100 mg qd po x 1 year
Placebo qd po x 1 year
LD-CT scan

1º Endpoint: #/Size semisolid lung nodules
2º Endpoints: COX/LOX urinary metabolites (hs-CRP, PGEM, LTE4), miRNA signature, nodule-based endpoints

Accrual as of October 15, 2015: 47 participants
Myo-Inositol

- Glucose isomer
- Source of several second messengers & signaling molecules
- Dietary sources (grains, beans, fruits, rice)
- Studied in psychiatric conditions (+/-), diabetic neuropathy (+/-), polycystic ovary syndrome (+)
Rationale for *myo*-Inositol in Lung Cancer Prevention

**Efficacy**
- Multiple animal studies show inhibition of carcinogen induced tumors in mice (40-50%)
  - Estensen and Wattenberg, Carcinogenesis 1993;14:1975
  - Hecht et al., Carcinogenesis 2002;23:1455
- Inhibits carcinogenesis in mainstream/sidestream smoke-exposed A/J mice by 53%
  - Witschi H et al., Carcinogenesis 1999;20:1375
- Combination with budesonide ↑↑ efficacy up to 80%
  - Estensen and Wattenberg, Carcinogenesis 1993;14:1975
  - Witschi et al. Carcinogenesis 1999;20:1375

**Safety**
- Used in multiple short term trials for psychiatric and diabetic neuropathy indications – no toxicity reported
- Generally Regarded as Safe (GRAS) by US FDA terminology
Phase I Study of myo-Inositol in Bronchial Dysplasia

- Inhibits B[a]P carcinogenesis in mice (53%); combination with budesonide ↑↑
- Phase I study (26 participants)
  - tolerable 18 g/d
  - 91% vs. 48% regression dysplasia, P=0.014 (10 participants)

Table 5. Changes in pathologic grades of bronchial biopsy samples at baseline and after 3 months of myo-inositol (18 g): Lesion-specific analysis

<table>
<thead>
<tr>
<th>Pathologic grades of bronchial biopsies at baseline</th>
<th>Status after 3 months of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Placebo group (from ref. 18)</td>
<td></td>
</tr>
<tr>
<td>Normal/hyperplasia/metaplasia</td>
<td>256</td>
</tr>
<tr>
<td>Mild dysplasia</td>
<td>134</td>
</tr>
<tr>
<td>Moderate/severe dysplasia</td>
<td>13</td>
</tr>
<tr>
<td>myo-Inositol group</td>
<td></td>
</tr>
<tr>
<td>Normal/hyperplasia/metaplasia</td>
<td>38</td>
</tr>
<tr>
<td>Mild dysplasia</td>
<td>10</td>
</tr>
<tr>
<td>Moderate/severe dysplasia</td>
<td>1</td>
</tr>
</tbody>
</table>

Lam et al., CEBP 2006;15:1526
PI3K pathway genes

Increased Expression of Genes Induced by PI3K Pathway Activation in the Airway of Smokers with Dysplasia

- PI3K pathway is activated in smokers with dysplasia in airway  p<0.001
- Myo-inositol inhibited PI3K activation in normal bronchial airways in smokers with regression of dysplasia (p=0.04)
Implications – Molecular Selection Criteria &/or Endpoints

• Does PI3K activation truly identify smokers at risk for cancer?
  – Easier to get normal brushings than to identify dysplasia (sampling bias); do not remove biomarker with procedure
  – Potential to identify “the right” cohort

• New potential clinical trial model – pathway analysis pre- and post-treatment, smaller # participants, shorter interventions
  – Identify mechanisms of interventions
  – Needs validation!
Phase IIB myo-Inositol Trial

Phase IIB myo-Inositol Trial Flow Diagram

11/2008 – 8/2013
448 Smokers Age 45-74; ≥30 pack-yrs

Bronchoscopy, Biopsy, Brush BAL
N = 332

≥1 Dysplasia Lesion N = 106

85/106 (83%) Randomized

Myo-inositol (A)
N = 44

Placebo (B)
N = 41

85 Evaluable for Intent To Treat Analysis

74 (A:38; B:36) Evaluable for Primary & Secondary Endpoints

No post-bronchoscopy N=6

No post-bronchoscopy N=5
Primary endpoint

Primary Endpoint

![Chart showing the percentage of participants in different groups and response categories for all subjects and subgroups of mild and moderate/severe dysplasia.](chart_image)

- All subjects
- Mild dysplasia
- Moderate or Severe Dysplasia

- Myo-Inositol
- Placebo

- Progressive Disease
- Stable Disease
- Partial Response
- Complete Response
Akt activation

AKT Pathway Activation is decreased in Myo-inositol Complete Responders
Summary

• Compared with placebo, myo-inositol 9 g BD x 6 m:
  - significant reduction of IL-6 and borderline significant reduction of myeloperoxidase levels in BAL
  - significant reduction of AKT pathway activation in complete responders

• Heterogeneous response in regression and progression of dysplasia

• Results suggested a targeted therapy approach based on molecular alterations is needed in future clinical trials
Lung Carcinogenesis

The Continuum of Lung Carcinogenesis
Opportunities for Intervention

Normal → Hyper/Metaplasia → Dysplasia → Early-Late Cancer

Prevention

Early Detection

Treatment
Issues in Lung Cancer Screening

• Lead-time bias=earlier diagnosis but no postponement of death (survival appears longer)
• Length bias=diagnosis of more indolent disease with longer preclinical phase (better prognosis, better outcome)
• Overdiagnosis=identification of clinically unimportant lesions that would not be diagnosed otherwise

• Morbidity/mortality/cost of screening and subsequent
PLCO Trial

PLCO CXR Randomized Trial - Mortality

154,901 participants, PA CXR vs. usual care x 4 screens, 13 yr f/u

Oken, MM et al. JAMA 2011;306:1865-73
NLST (National Lung Screening Trial)

• NLST design
  – 53,454 smokers (current and former)
  – 30 pack-yr smoking hx; quit ≤15 yrs ago
  – Age 55-74
  – Helical CT vs. chest X-ray (prevalence, then x2)

• NLST results
  – CT - 24.2% ‘positive’ tests, 354 lung cancer deaths
  – CXR – 6.9% ‘positive’ tests, 442 lung cancer deaths
  – 20.0% reduction in lung cancer mortality
  – 6.7% reduction in all cause mortality

Lung Cancer and Deaths

Cumulative Lung Cancers and Deaths from Lung Cancer

Lung Cancer Risk

Lung Cancer Risk Prediction Model – 1st Screening CT

- Risk of lung cancer in nodules from baseline screening CT
  - Age, sex, family history, emphysema
  - Nodule size, type, location, count
  - AUC >0.90

- Ability to identify highest risk:
  - For subsequent screening
  - Chemoprevention (ph III)

www.brocku.ca/cancerpredictionresearch

Moving forward

How do we move forward?

- Understand the genesis and natural history of carcinogenesis
  - Understanding molecular mechanisms of carcinogenesis, TCGA of premalignancy (PCA)
    - Molecularly targeted agents
    - Repurposed ‘old’ drugs
    - Target deregulated processes driving carcinogenesis
    - Harness the immune response
  - Persistent versus regressive premalignant lesions - who is likely to progress and why?
Innovation trial designs

How do we move forward?

Innovative Trial Designs

• Sample the field using ‘omic’ technologies
  – To detect drug effects on deregulated pathways in a short time frame

• Focus on at-risk (molecularly?) homogeneous cohorts

• Multiple trial designs to build a “body of evidence”

-Gustafson et al. Sci Transl Med 2010;2:26ra25
Summary

Tremendous progress has been made in understanding lung carcinogenesis

- Precision medicine applicable to significant (but small) subset of advanced stage patients, increased survival
- Early days of immunotherapy – prolonged survival in small subset of patients
- Early detection with helical CT – decreased lung cancer mortality
- New targets and tools available for chemoprevention research
“An ounce of prevention is worth a pound of cure”
-Benjamin Franklin
Acknowledgments

- DCP Phase II Consortia Program
- Stephen Lam, British Columbia Cancer Agency
- Giulia Veronesi, Humanitas Cancer Institute
- European Institute of Oncology Chemoprevention Group
- Ron Lubet, DCP CADRG
- Avrum Spira, Boston University