The WIN consortium BOOSTER trial for identification and validation of new blood biomarkers for NSCLC

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Disclosures

I have nothing to disclose
BOOSTER: Biomarkers in Oncology for Overall Survival and Therapeutic Efficacy Repository
Focus on lung cancer – look for biomarkers for early detection and monitoring the course of the disease
Lung cancer is the most common cancer in the world:

1.8x10^6 new cases in 2012 (13% of the total), 58% in the less developed regions.

The most common cancer in men worldwide (1.2 million, 16.7% of the total), highest incidence in Central and Eastern Europe (53.5 per 100,000) and Eastern Asia (50.4 per 100,000).

In women, the incidence rates are lower reflecting different historical exposure to tobacco smoking.

Lung cancer is the most common cause of death from cancer worldwide: 1.59x10^6 deaths, 20% of the total.
International Agency for Research on Cancer

http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
Why can’t we do better for such a common disease?
Heterogeneity
<table>
<thead>
<tr>
<th>Class</th>
<th>Prevalence (%)</th>
<th>Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>40</td>
<td>Acinar, bronchioalveolar, papillary, solid carcinoma with mucus formation, mixed</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>25</td>
<td>—</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>20</td>
<td>Pure small cell carcinoma, combined small cell carcinoma</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>10</td>
<td>Large cell neuroendocrine, basaloid, lymphoepithelial-like, large cell with rhabdoid phenotype</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
<td>&lt; 5</td>
<td>—</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>&lt; 5</td>
<td>—</td>
</tr>
<tr>
<td>Bronchial gland carcinoma</td>
<td>&lt; 5</td>
<td>—</td>
</tr>
</tbody>
</table>
NSCLC, the Most Common Type of Lung Cancer, Is Genomically Diverse

Types of Lung Cancer

- SCLC 15%
- NSCLC 85%

Types of NSCLC

- Adeno-carcinoma 55%
- Squamous 34%
- Other 11%

Driver Mutations in Adenocarcinoma

- ALK
- HER2
- BRAF
- PIK3CA
- AKT1
- MAP2K1
- NRAS
- RAS1
- RET
- EGFR
- KRAS
- Unknown

Driver Mutations in Squamous Cell Carcinoma

- EGFRvIII
- PI3KCA
- EGFR
- DDR2
- FGFR1 Amp
- Unknown

FIGURE 2. Overall survival curves according to the histological subtype (N = 427: Adenoca = 346 and SQ = 81, P < 0.001).

Medicine • Volume 95, Number 6, February 2016
What are the limitations of imaging studies?
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team

ABSTRACT

BACKGROUND
The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

METHODS
From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to un-
The NSLT program

• A study to early detect lung cancer in high risk individuals (=smokers or ex-smokers)

• Annual low-dose radiation CT vs CXR

• A reduction in lung cancer related death and overall death in the CT group
The NSLT program

- 26,000 cases underwent annual thoracic low-dose CT
- In 25% positive findings (nodules) were detected
- But 98% of them were not cancer
- App 350 CTs to detect one patient with lung cancer
Implementation of Lung Cancer Screening in the Veterans Health Administration

Linda S. Kinsinger, MD, MPH; Charles Anderson, MD, PhD; Jane Kim, MD, MPH; Martha Larson, BSN, MS; Stephanie H. Chan, MPH; Heather A. King, PhD; Kathryn L. Rice, MD; Christopher G. Slatore, MD, MS; Nichole T. Tanner, MD, MSCR; Kathleen Pittman, BSN, MPH; Robert J. Monte, MBA; Rebecca B. McNeil, PhD; Janet M. Grubber, MSPH; Michael J. Kelley, MD; Dawn Provenzale, MD, MSc; Santanu K. Datta, PhD; Nina S. Sperber, PhD; Lottie K. Barnes, MPH; David H. Abbott, MS; Kellie J. Sims, PhD, MS; Richard L. Whitley, BS; R. Ryanne Wu, MD, MHS; George L. Jackson, PhD, MHA

**IMPORTANCE** The US Preventive Services Task Force recommends annual lung cancer screening (LCS) with low-dose computed tomography for current and former heavy smokers aged 55 to 80 years. There is little published experience regarding implementing this recommendation in clinical practice.

**OBJECTIVES** To describe organizational- and patient-level experiences with implementing an LCS program in selected Veterans Health Administration (VHA) hospitals and to estimate the number of VHA patients who may be candidates for LCS.

Real life experience with low-dose CT for early detection of lung cancer – the VA experience

• Only 60% of patients that were qualified agreed to participate

• In 60% of the cases a nodule was detected

• Obviously we need additional technologies
Why don’t we use blood-born or tissue markers?
Detection and localization of surgically resectable cancers with a multi-analyte blood test

Joshua D. Cohen,1,2,3,4,5 Lu Li,6 Yuxuan Wang,1,2,3,4 Christopher Thoburn,3 Bahman Afsari,7 Ludmila Danilova,7 Christopher Douville,1,2,3,4 Ammar A. Javed,8 Fay Wong,1,3,4 Austin Mattox,1,2,3,4 Ralph. H. Hruban,3,4,9 Christopher L. Wolfgang,8 Michael G. Goggins,3,4,9,10,11 Marco Dal Molin,4 Tian-Li Wang,3,9 Richard Roden,3,9 Alison P. Klein,3,4,12 Janine Ptak,1,2,3,4 Lisa Dobbyn,1,3,4 Joy Schaefer,1,3,4 Natalie Silliman,1,2,3,4 Maria Popoli,1,3,4 Joshua T. Vogelstein,13 James D. Browne,14 Robert E. Schoen,15,16 Randall E. Brand,15 Jeanne Tie,17,18,19,20 Peter Gibbs,17,18,19,20 Hui-Li Wong,17 Aaron S. Mansfield,21 Jin Jen,22 Samir M. Hanash,23 Massimo Falconi,24 Peter J. Allen,25 Shibin Zhou,1,3,4 Chetan Bettegowda,1,3,4 Luis A. Diaz Jr.,1,3,4 Cristian Tomasetti,3,6,7† Kenneth W. Kinzler,1,3,4† Bert Vogelstein,1,2,3,4† Anne Marie Lennon,3,4,8,10,11† Nickolas Papadopoulos1,3,4†

**Fig. 1. Development of a PCR-based assay to identify tumor-specific mutations in plasma samples.** Colored curves indicate the proportion of cancers of the eight types evaluated in this study that can be detected with an increasing number of short (<40 bp) amplicons. The sensitivity of detection increases with the number of amplicons but plateaus at ~60 amplicons. Colored dots indicate the fraction of cancers detected by using the 61-amplicon panel used in 805 cancers evaluated in our study, which averaged 82%. Publicly available sequencing data were obtained from the COSMIC repository.
So how would BOOSTER make a difference?
Very few biomarkers: PSA, AFP, CEA, CA 19-9, CA 125, CA 15,3, hCH, bhCG

For Lung cancer: A panel of biomarkers is likely to be necessary to cover all patients, rather than a single marker.

→ The community needs an effective global platform to validate biomarker candidates and increase chances of identifying a panel of efficacious markers.
WIN OFFERS A « FACTORY » FOR BIOMARKER VALIDATION

4,000 patients:
- USA & Europe
- China, Korea
- India
- Jordan and Israel

- 4,000 fully characterized NSCLC Stage I patients
- Sequential liquid biopsies → Each patient is his own control
- Biomarker must be positive before surgery and negative after complete removal of the tumor
- Accelerate considerably power of analyses and represent a very effective way to circumvent the hurdles met by traditional large cohort studies.

- Open platform to any institution (academic or industry inside and outside WIN)
- Enables identification and validation of panels of several biomarkers (coming from different institutions)
Thank you for your attention

For additional information please contact

• Amir Onn

• WIN leadership