CHALLENGES OF TISSUE ACQUISITION AND BIOMARKER TESTING IN COMMUNITY AND AND ACADEMIC SETTINGS

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DISCLOSURES

| Source | Research Funding | Consulting |
|--------------------------|------------------|------------|
| Auris Medical | X | Х |
| Biodesix | Х | Х |
| Exact Sciences | Х | |
| Oncocyte | Х | |
| Olympus | Х | Х |
| PCORI | Х | |
| Veran medical | X | |
| NIH NCI | X | |
| Aries pharmaceutical | X | |
| Boston Scientific | Х | |

Spectrum of (Lung) Cancer Biomarkers

Nodule Risk Stratification Mutational Analysis For Advanced Disease

Response to Treatment

Screening

Risk of Recurrence

Disease Monitoring

Lest we forget... from whence we came



1.0 Median; 95% CI 1.0 Median; 95% Cl Arvival Probability 0.8 0.6 0.6 0.4 0.3 0.2 0.4 0.2 0.9 - CP 10.3; 9.8, 11.2 - CP 4.8; 4.6, 5.3 10.3; 9.6, 10.9 5.1; 4.6, 5.5 CG CG Adjusted HR; 95% CI CP v CG Adjusted HR; 95% CI CP v CG 0.94; 0.84, 1.05 1.04; 0.94, 1.15 PFS 0.3 0.2 0.1 0.1 18 12 0 12 24 0 18 24 30 6 30 PFS (months) in All Patients Survival Time (months) in All Patients 1.0 Median: 95% CI Median: 95% CI 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.4 0.3 0.2 0.1 0.9 0.9 11.8; 10.4, 13.2 5.3; 4.8, 5.7 - CP - CP Probability 9.0 0.2 0.4 0.4 4.7; 4.4, 5.4 CG 10.4; 9.6, 11.2 CG Adjusted HR; 95% CI CP v CG Adjusted HR; 95% CI CP v CG 0.81; 0.70, 0.94 0.90; 0.79, 1.02 SHO 0.3 0.1 0 12 18 24 30 0 6 12 18 24 30 6 Survival Time (months) in Patients PFS (months) in Patients With Nonsquamous Histology With Nonsquamous Histology 1.0 1.0 Median: 95% CI Median: 95% CI 0.9 CP 9.4; 8.4, 10.2 4.4; 4.1, 4.9 PFS Probability - 2.0 - 7.0 - 10.8; 9.5, 12.1 5.5; 4.6, 5.9 CG CG CP v CG Adjusted HR; 95% CI Adjusted HR: 95% CI CP v CG 1.23; 1.00, 1.51 1.36; 1.12, 1.65 0.1 0.1 12 18 24 30 12 18 24 30 0 0 PFS (months) in Patients Survival Time (months) in Patients With Squamous Cell Carcinoma With Squamous Cell Carcinoma

Schiller JH, et al. N Engl J Med 2002, 246:92

Scagliotti GV et al. J Clin Oncol 2008, 26:3543

Non-Squamous Non-Small Cell Lung Cancer Biomarkers



Pao and Hutchinson 'Chipping away at the lung cancer genome' Nature Medicine. <u>March 2012</u> Scholl et al. Lung Cancer Mutation Consortium J Thorac Oncol. <u>May 2015</u>

<u>2020</u>: biomarkers with drug targets

On Erlotinib 3 months





Biomarkers for Lung Cancer Treatment

| Target | Prevalenc e | Initial FDA Approval | Drugs |
|------------------------|----------------|-------------------------|---|
| EGFR | 10-15% | 2003 | Gefitinib, Erlotinib, Afatinib, Osimertinib, |
| ALK | 2-7% | 2011 | Crizotinib, Ceritinib, Alectinib, Lorlatinib, Brigantinib, |
| ROS-1 | 1-2% | 2016 | Crizotinib, Entrectinib, Ceritinib, Lorlatinib |
| PD-L1 TPS 50% | 30% | 2016 | Pembrolizumab, Atezolizumab |
| B-RAF ^{V600E} | 2% | 2017 | Dabrafenib+Trametinib, Vemurafenib |
| NTRK | 0.2-3% | 2018 | Larotrectinib, Entrectinib |
| HER-2 (ERBB2) | 2-5% | May 2020 | Trastuzumab deruxtecan (Enhertu) |
| MET exon 14 skipping | 3-4% | May 2020 | Capmatinib; ?Tepotinib?, Crizotinib |
| RET | 1-2% | September 4, 2020 | Salpercatinib, Pralsetinib, Carbozantinib, Vandetanib |
| K-RAS G12C | 12% | 2021 | sotorasib |

PERSONALIZED MEDICINE FOR NSCLC

Limitations in understanding current US trends:

- Complexity of the US healthcare system with many payers and numerous health systems
- Constantly growing number of biomarkers with actionable therapies
- Constantly evolving evidence and indications for testing and use target and immunotherapies



Simplified timeline of Biomarkers with FDA Approved Therapies

Gutierrez et al.

- 89 oncologists and 15 community oncology sites, 814 patients
- Death within 30 days and active smoking were tested less frequently.
- Gender, age, race, referral vs community center, and practice size had no effect on testing rate

Biomarker testing rates:

- EGFR 69% MET 15%
 - ALK 65% RET 14%
 - ROSI 25% HER2 12%
- BRAF 18%



John et al.

- Retrospective analysis of non-squamous NSCLC in Flatiron health record database
- ~15,000 patients at 450 sites across 25 US States
- Omits ~2,000 without any testing*
- Primary outcome was looking at effect of treatments

*Biomarker testing rates:

- EGFR 93.4% (n = 13,767)
- ALK 86.0% (n = 12,671)
- ROSI 43.5% (n = 6,410)
- PD-LI 28.4% (n = 4,182)
- BRAF 25.5% (n = 3,757)



Mason et al.

- Retrospective analysis of 7 cancer centers in the U.S., both academic and community settings
- ~300 patients
- Provider-entered information into the electronic health record

Biomarker testing rates:

- EGFR 95% (n = 288)
- ALK 94% (n = 285)
- ROSI 88% (n = 267)



Waterhouse et al.

- Retrospective analysis of a network 450 sites of community oncology care across 25 U.S. States
- 3,337 patients identified, but had to have followup visits and not be involved in any clinical trials
- Relies on information entered manually into the health record*

*Biomarker testing rates:

- EGFR 36%
- ALK 35%
- ROSI 20%
- BRAF 16%
- PD-LI 37%



Reported Biomarker Testing Rates by Region



Common Diagnostic Pathway in Advanced Lung Cancer



How often do pulmonologists encounter advanced lung cancer in their practice?



How often are pulmonologists ordering biomarker testing?



What assays and testing strategies do they use?



Do pulmonologists perform or have access to technology such as EBUS and ROSE?



What do pulmonologists know about individual biomarkers and therapies?

PULMONOLOGISTS ROLE IN BIOMARKER TESTING

- Cross-sectional survey of over 450 pulmonologists in the CHEST database
- Study period April-May 2019
- Key question domains:
 - Practices for diagnosing advanced lung cancer
 - Collaboration between sub-specialties
 - Knowledge of individual biomarkers





Number of Needle Passes During EBUS to Collect Tissue for Biomarker Testing



- Responsible for ordering:
 - Oncologists (37%)
 - Pathologists (31%)
 - Pulmonologists (23%)
 - Tumor board (7%)
- 48% reported an institutional policy to guide biomarker testing
- Location:
 - In-house (20%)
 - Outside testing (44%)
 - Combination (31%)



KEY MESSAGES

- Assessing success of biomarker testing is limited by data quality and pace of development
- Practices for performing biomarker testing are variable
- Successful biomarker testing requires coordination across several sub-specialties
- Pulmonologists play a central role

FUTURE DIRECTIONS

- Turn around time
- Liquid biopsy
- Reflex testing
- Testing for surgically resectable disease
- Who is not being tested or treated.