

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	X
Biodesix	X	X
Exact Sciences	X	
Oncocyte	X	
Olympus	X	X
PCORI	X	
Veran medical	X	
NIH NCI	X	
Aries pharmaceutical	X	
Boston Scientific	X	

Spectrum of (Lung) Cancer Biomarkers

Nodule Risk Stratification

Mutational Analysis For Advanced Disease

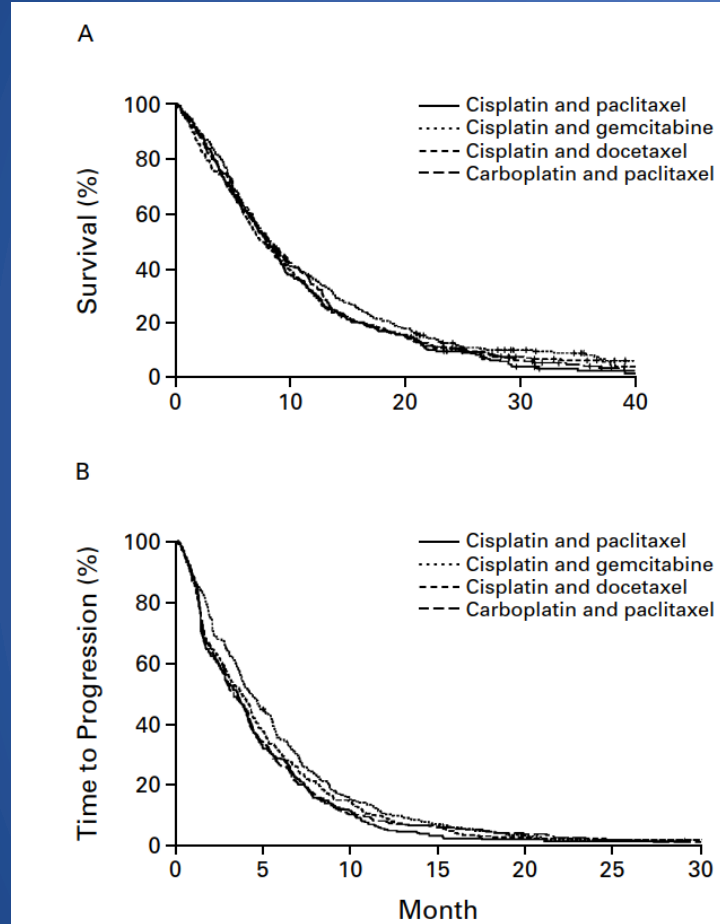
Response to Treatment

Screening

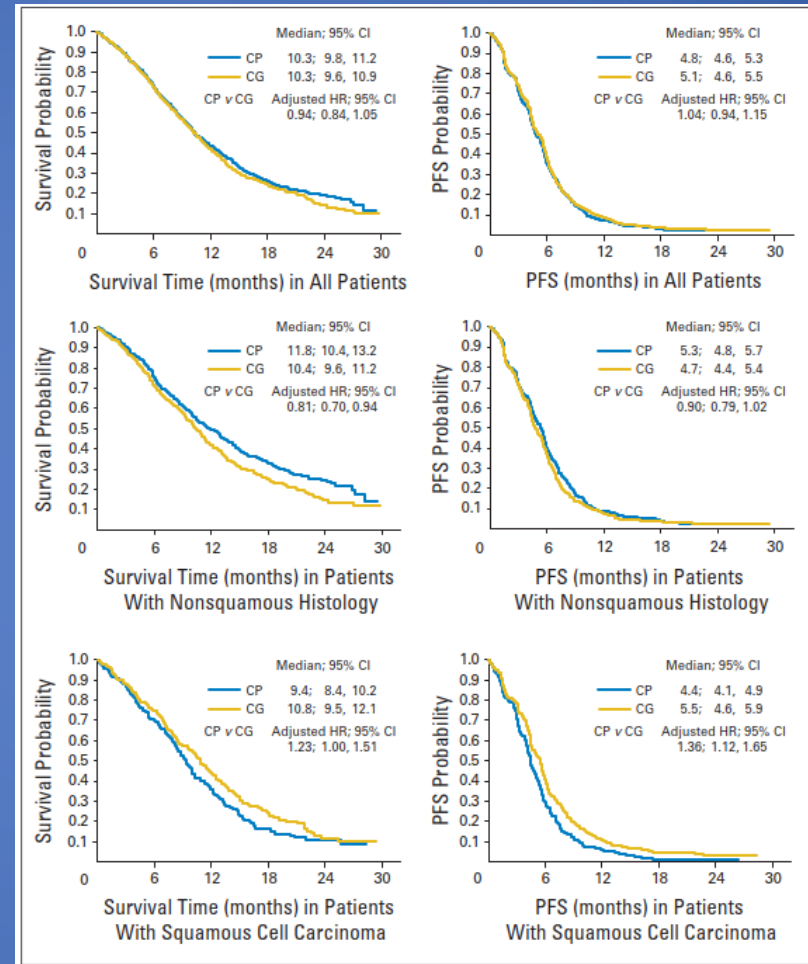
Risk of Recurrence

Disease Monitoring

Lest we forget... from whence we came

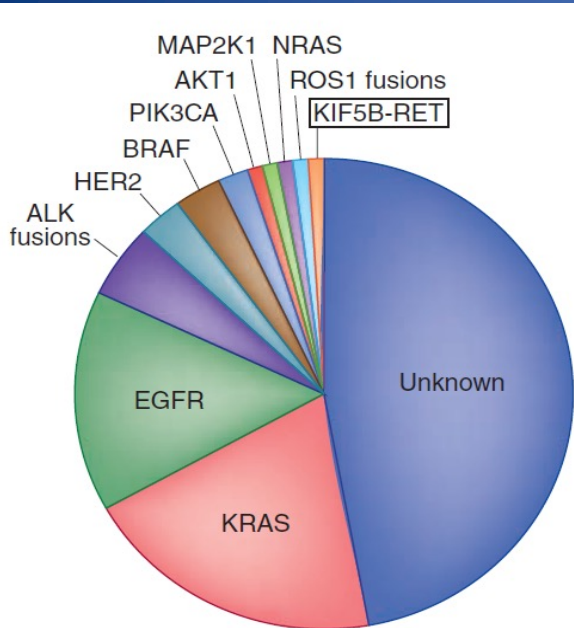


Schiller JH, et al. N Engl J Med 2002, 246:92

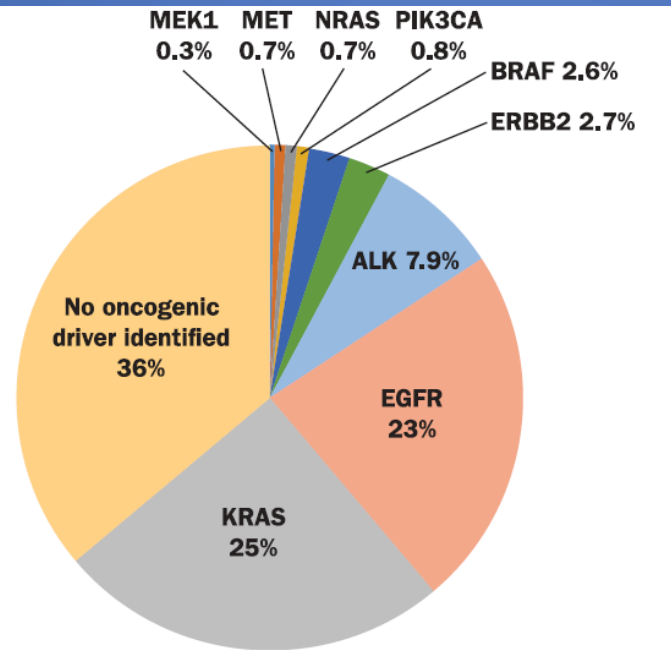


Scagliotti GV et al. J Clin Oncol 2008, 26:3543

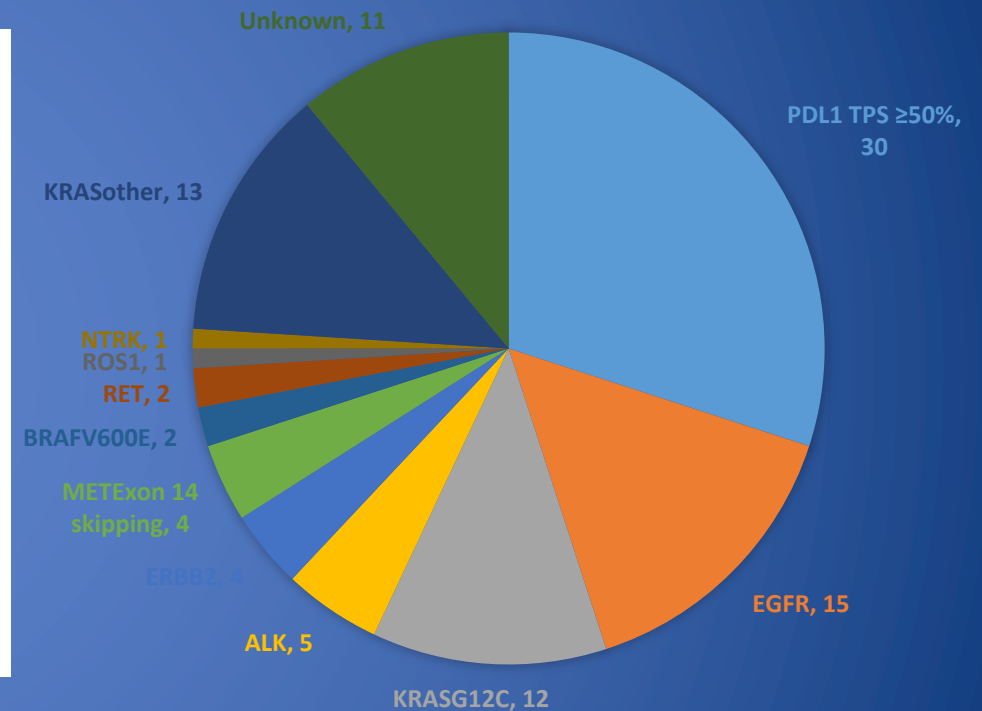
Non-Squamous Non-Small Cell Lung Cancer Biomarkers



Pao and Hutchinson 'Chipping away at the lung cancer genome' Nature Medicine. March 2012

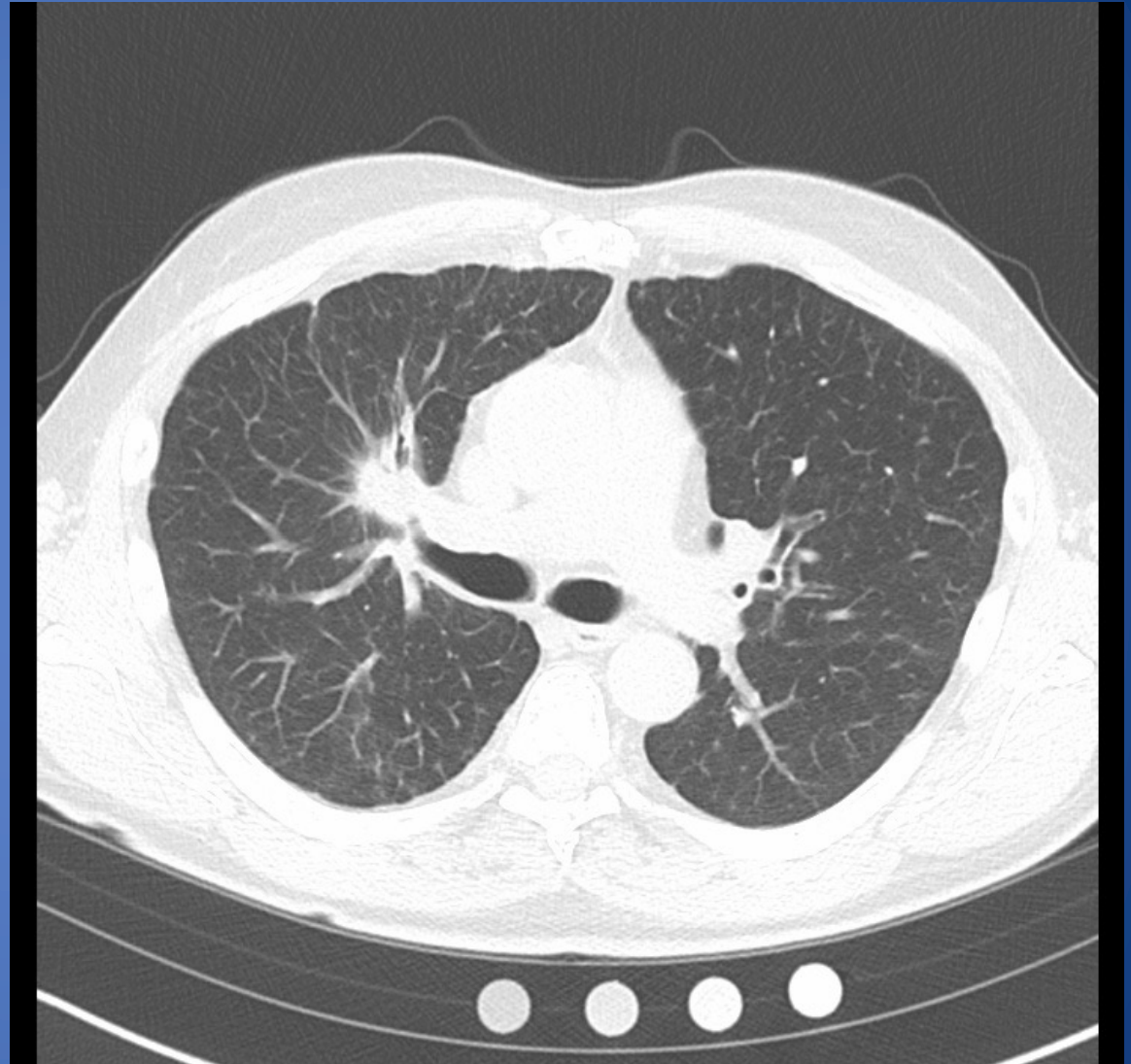
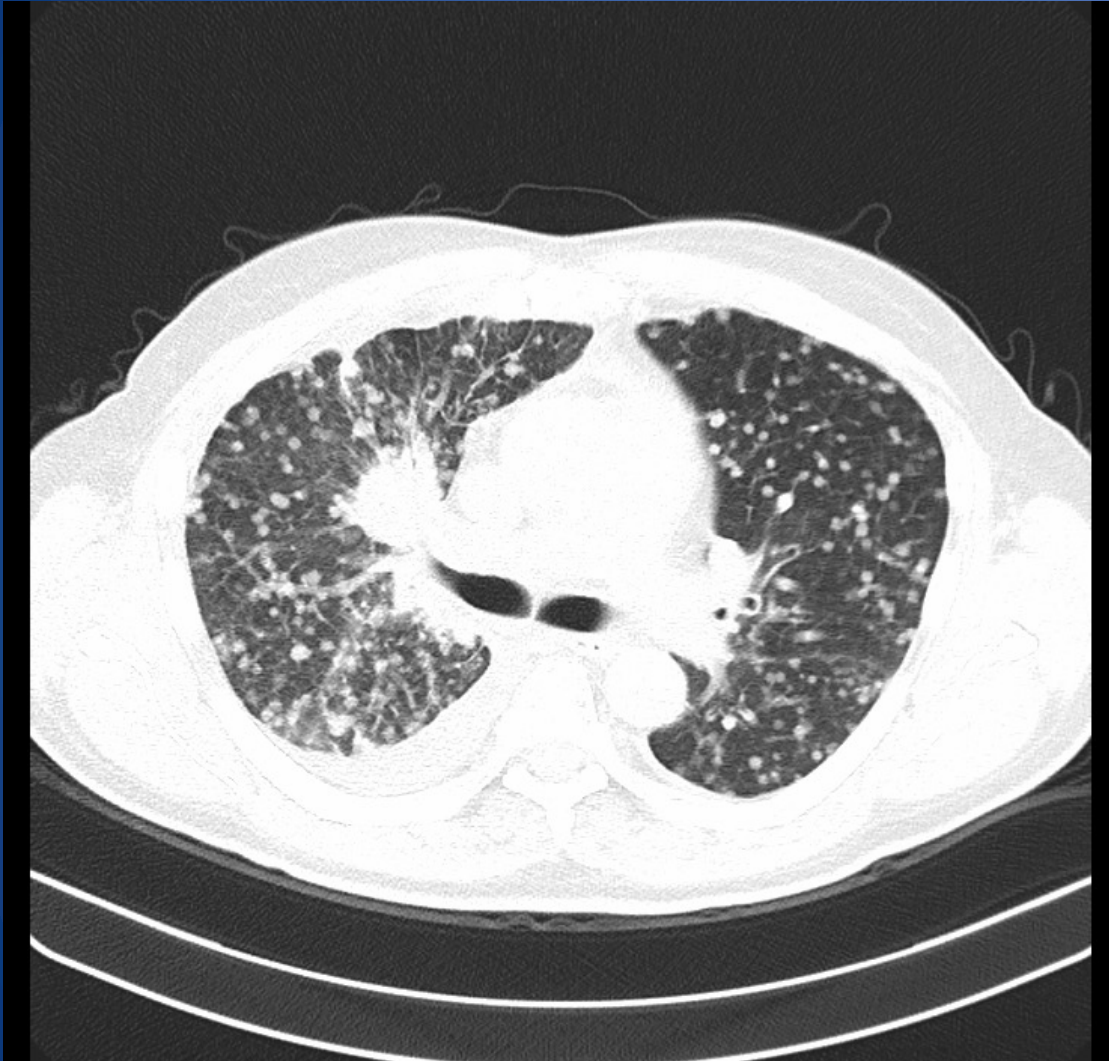


Scholl et al. Lung Cancer Mutation Consortium J Thorac Oncol. May 2015



2020: biomarkers with drug targets

On Erlotinib 3 months



Biomarkers for Lung Cancer Treatment

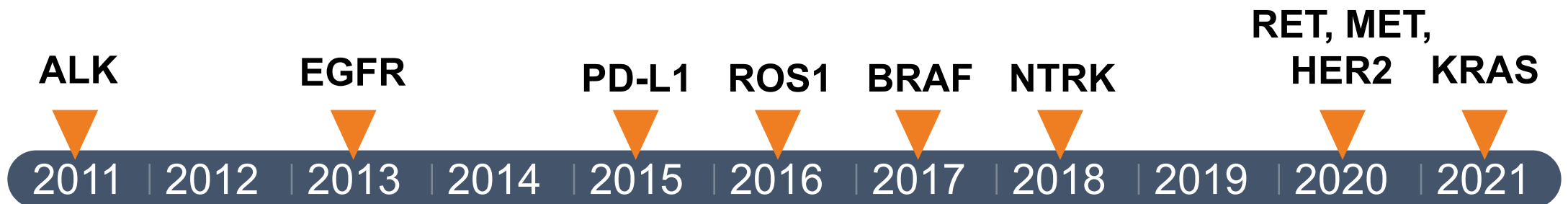
Target	Prevalence	Initial FDA Approval	Drugs
EGFR	10-15%	2003	Gefitinib, Erlotinib, Afatinib, Osimertinib,
ALK	2-7%	2011	Crizotinib, Ceritinib, Alectinib, Lorlatinib, Brigantiniib,
R0S-1	1-2%	2016	Crizotinib, Entrectinib, Ceritinib, Lorlatinib
PD-L1 TPS 50%	30%	2016	Pembrolizumab, Atezolizumab
B-RAF^{V600E}	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	<u>sotorasib</u>

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



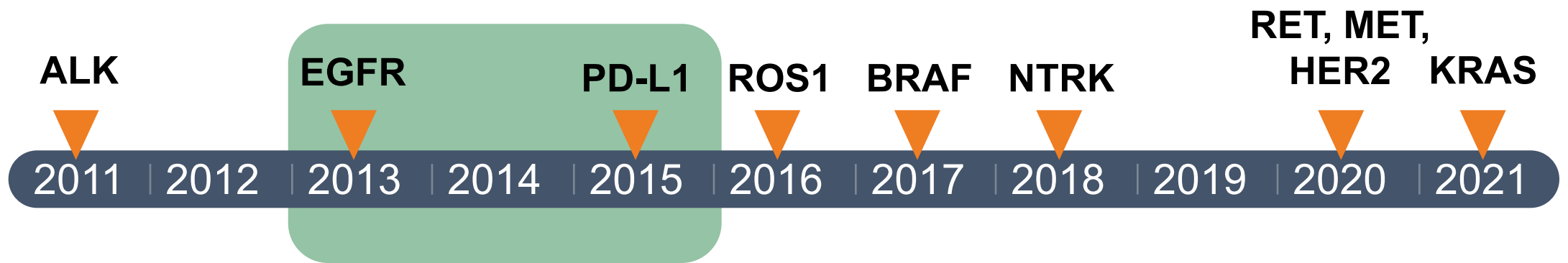
BIOMARKER TESTING RATES IN THE US

Gutierrez et al.

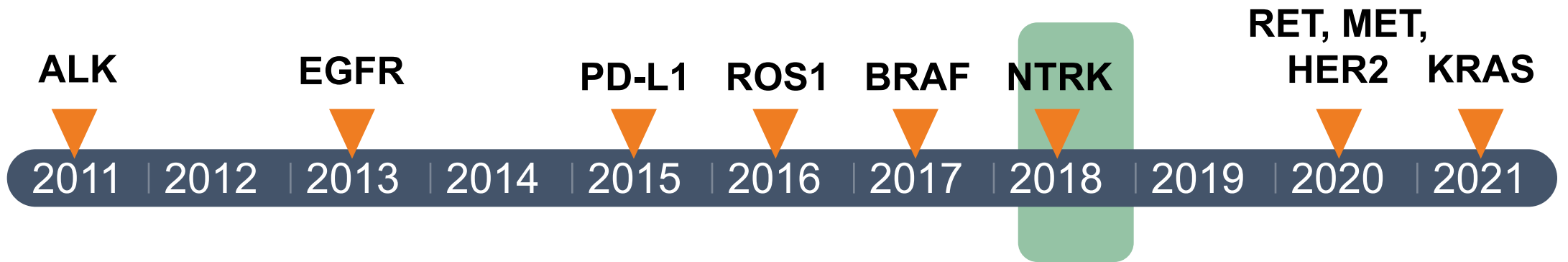
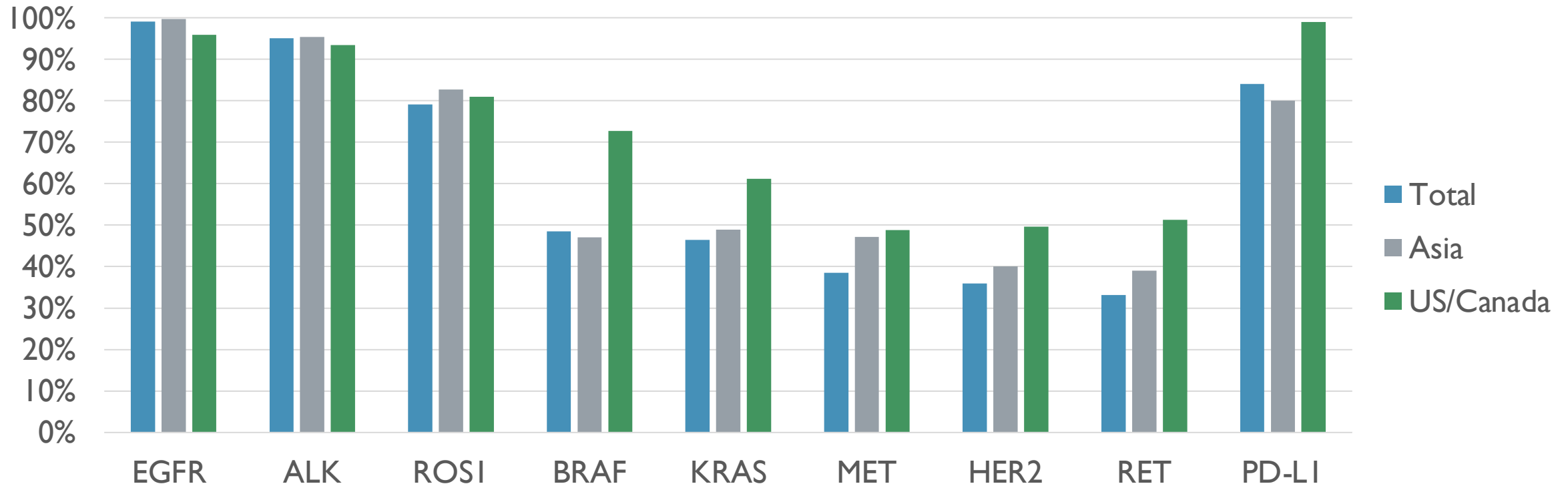
- 89 oncologists and 15 community oncology sites, 814 patients
- Death within 30 days and active smoking were tested less frequently.
- Gender, age, race, referral vs community center, and practice size had no effect on testing rate

Biomarker testing rates:

- EGFR 69%
- ALK 65%
- ROS1 25%
- BRAF 18%
- MET 15%
- RET 14%
- HER2 12%



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?



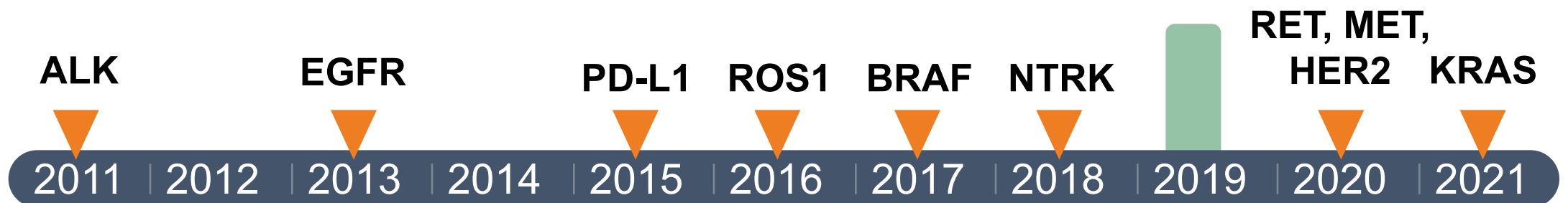
Do pulmonologists perform or have access to technology such as EBUS and ROSE?



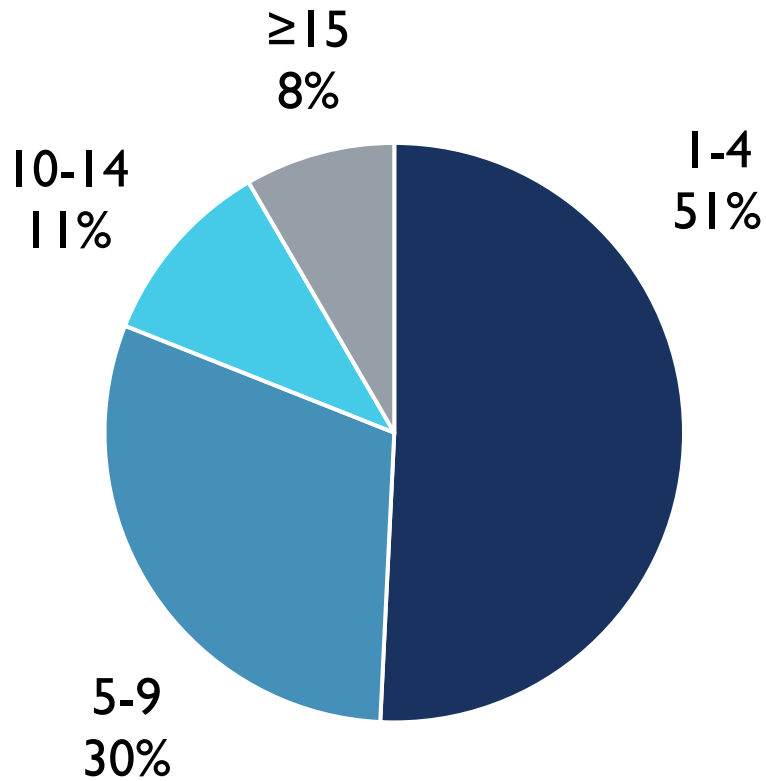
What do pulmonologists know about individual biomarkers and therapies?

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

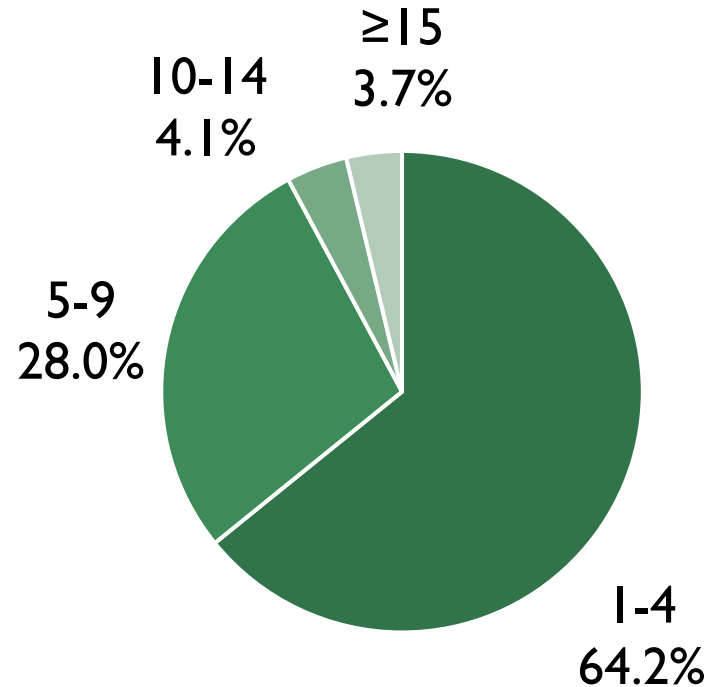


All Respondents
n = 453

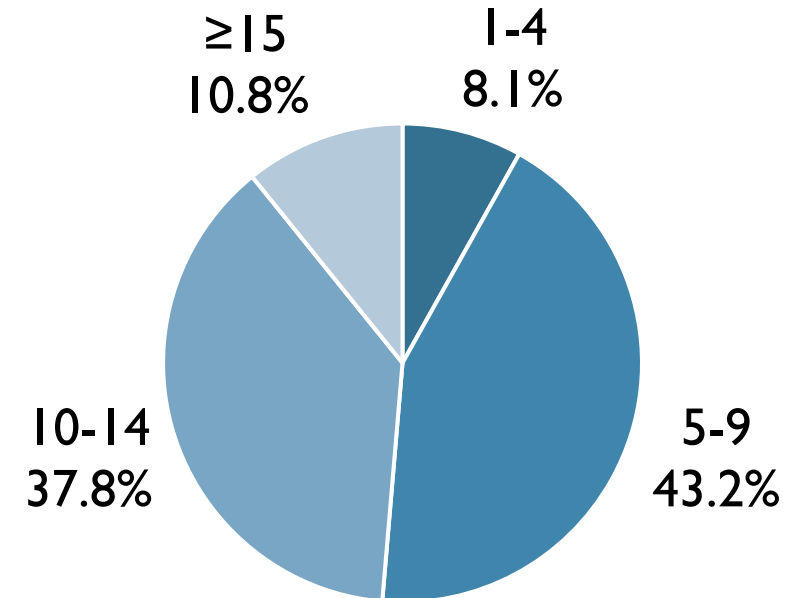


Number of New Patients with Lung Cancer Per Month

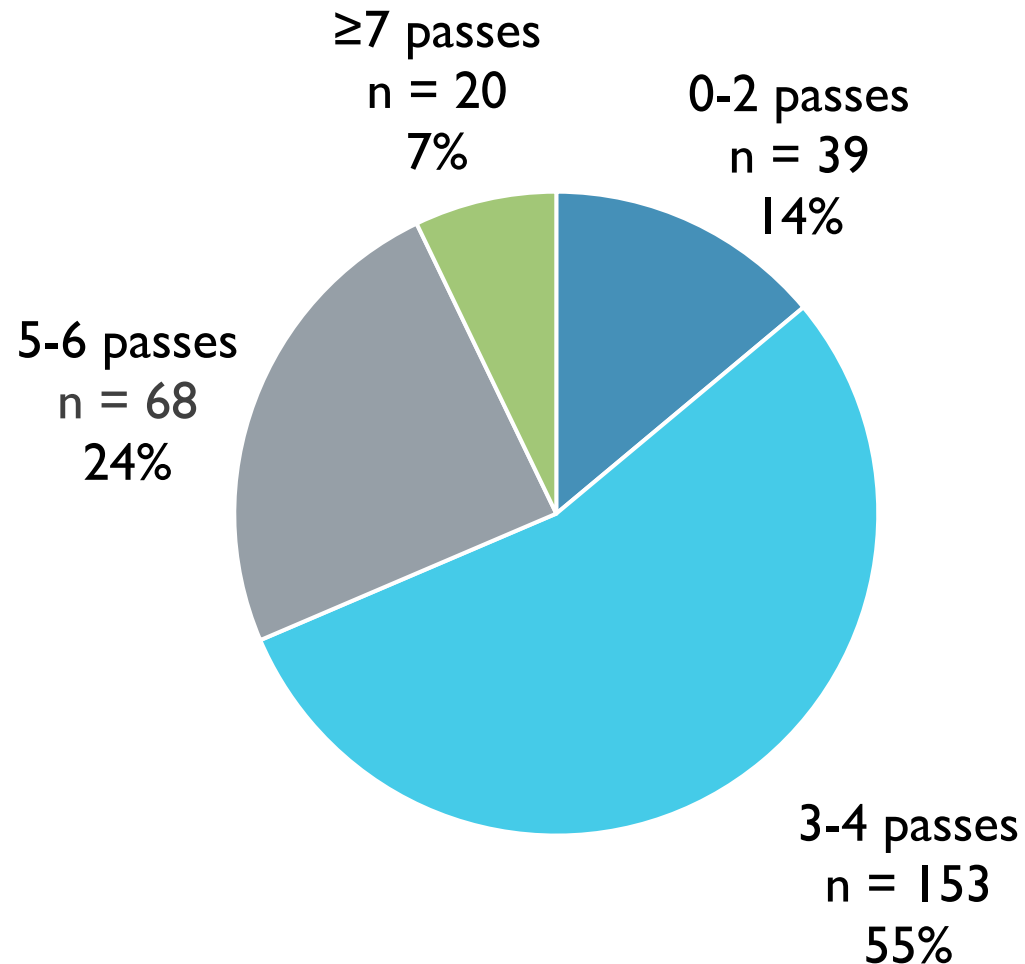
Community Generalists
n = 268



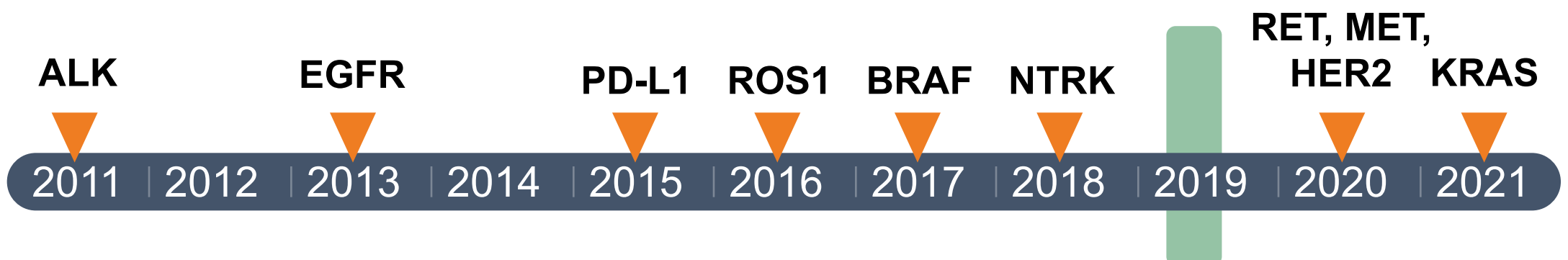
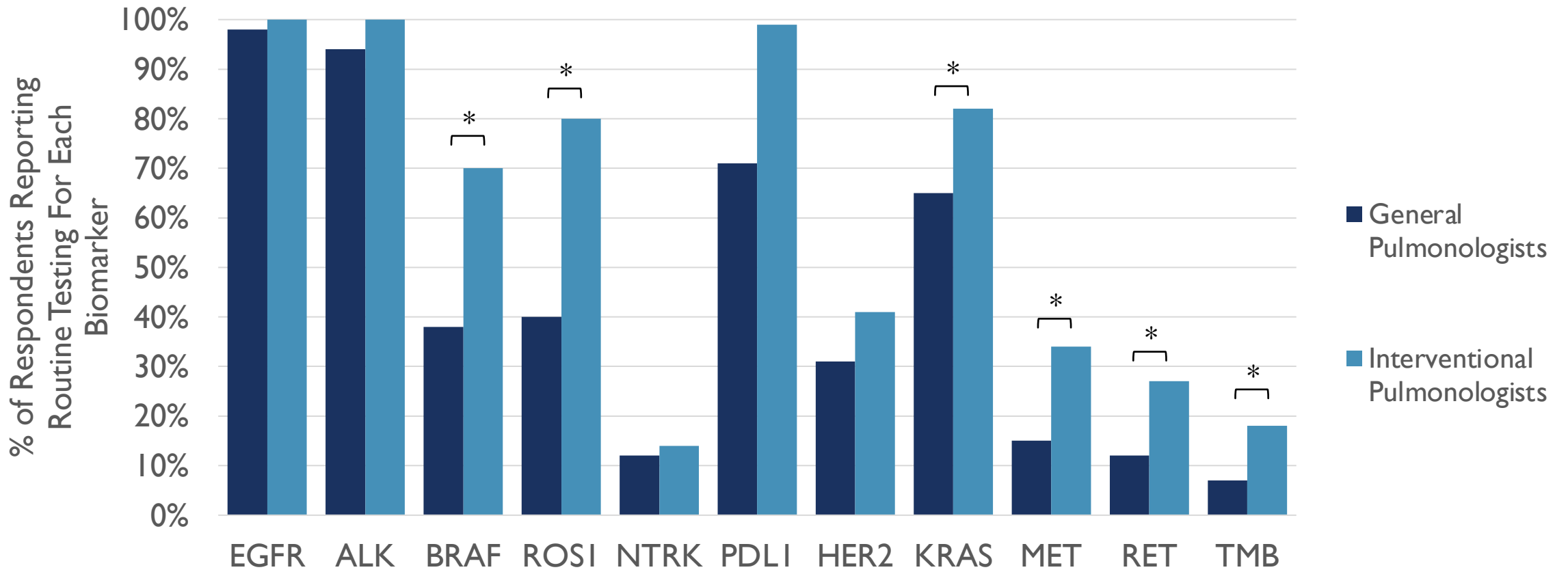
Community Interventionalists
n = 37



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.