LUNG CANCER PATIENT SUPPORT ECHO SESSION 7
VARIABILITY IN ACCESS TO AND USE OF MUTATIONAL TESTING FOR
EXPRESSION OF IMMUNE MARKERS AND TARGETED THERAPY

DAVID SPIGEL, MD
JENNIFER KING, PHD
GERARD SILVESTRI, MD
JOHN RUCKDESCHEL, MD  (FACILITATOR)

NOVEMBER 29, 2018
9:00 AM ET
# TODAY’S AGENDA

<table>
<thead>
<tr>
<th>Time</th>
<th>Presentation</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00-9:10</td>
<td>Welcome, roll call, housekeeping</td>
<td>John Ruckdeschel, MD</td>
</tr>
<tr>
<td>9:10-9:45</td>
<td>Didactic Presentation: ECHO Session 6</td>
<td>David Spigel, MD, Jennifer King, Ph.D., Gerard Silvestri, MD</td>
</tr>
<tr>
<td>9:45-10:00</td>
<td>Q &amp; A/Discussion</td>
<td>John Ruckdeschel, MD</td>
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<tr>
<td>10:00-10:15</td>
<td>Case Presentation/ Q&amp;A</td>
<td>David Spigel, MD</td>
</tr>
<tr>
<td>10:15-10:25</td>
<td>Small Grant Program Announcement</td>
<td>Dawn Wiatrek, Ph.D., Octavia Vogel, MPH</td>
</tr>
<tr>
<td>10:25-10:30</td>
<td>Conclusion/Next session</td>
<td>John Ruckdeschel, MD, Dawn Wiatrek, Ph.D., Octavia Vogel, MPH</td>
</tr>
</tbody>
</table>

*Sessions will be recorded.*

*Please mute phones when not speaking. Mute cell phones and try to reduce extraneous noise.*

*Remember to e-mail Octavia Vogel by 11/30 if you are requesting CME/CEU credit.*
UNM CME policy, in compliance with the ACCME Standards of Commercial Support, requires that anyone who is in a position to control the content of an activity disclose all relevant financial relationships they have had within the last 12 months with a commercial interest related to the content of this activity.

The following planners and faculty disclose that they have no financial relationships with any commercial interest: (next slide)
Lead Facilitator:  John Ruckdeschel, MD  
Director, University of Mississippi Cancer Center

Presenters:  
David Spigel, M.D.  
Chief Scientific Officer  
Director, Lung Cancer Research Program  
Sarah Cannon Health System

Jennifer King, Ph.D.  
Director, Science and Research  
Lung Cancer Alliance

Gerard Silvestri, M.D.  
Professor of Medicine  
Medical University of South Carolina

Case Presentation:  TBD
This session will provide an overview of the latest information on diagnostic follow up and biomarker testing for immunotherapy including reimbursement concerns, and other key topics.
MOLECULAR TESTING IN LUNG CANCER: NO LONGER WHY, BUT HOW

DAVID R. SPIGEL, M.D.
SARAH CANNON RESEARCH INSTITUTE
Disclosures

Research Grant – Funding to Institution:
• AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, F.Hoffmann-La Roche/Genentech/Foundation Medicine, GI Therapeutics, GlaxoSmithKline, Lilly, Merck, Neon, Novartis, Pfizer, Takeda

Advisory Board – Funding to Institution:
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UNDERSTANDING WHAT WE ARE TREATING

Shaw, NEJM 2014
Lung Cancer is the leading cause of cancer-related deaths. 1.6 million/year.

Nearly 3 out of 5 new patients with lung cancer will be from low/middle income countries (LMICs).
GLOBAL LUNG CANCER INCIDENCE

Torre, Cancer Epi, Bio, Prev 2016
GENOMIC ALTERATIONS IN NSCLC: PROJECT GENIE
Cancer Discovery, 2017
# BEST RECOMMENDATIONS TODAY

## Non-Small Cell Lung Cancer

### NCCN Guidelines Version 2.2019

#### CLINICAL PRESENTATION

**Advanced or metastatic Disease**

- Establish histologic subtype\(^a\) with adequate tissue for molecular testing (consider rebiopsy\(^\text{gb}\) if appropriate)
- Smoking cessation counseling
- Integrate palliative care\(^c\) (See NCCN Guidelines for Palliative Care)

#### HISTOLOGIC SUBTYPE\(^b\)

- Adenocarcinoma
- Large cell
- NSCLC not otherwise specified (NOS)

#### TESTING\(^{hh}\)

- Molecular testing
  - EGFR mutation testing (category 1)
  - ALK testing (category 1)
  - ROS1 testing
  - BRAF testing
  - Testing should be conducted as part of broad molecular profiling\(^{ii}\)
  - PD-L1 testing (category 1)

- Molecular testing
  - Consider EGFR mutation and ALK testing\(^{ij}\) in never smokers or small biopsy specimens, or mixed histology\(^{kk}\)
  - Consider ROS1 and BRAF testing in small biopsy specimens or mixed histology
  - Testing should be conducted as part of broad molecular profiling\(^{ii}\)
  - PD-L1 testing (category 1)

#### TESTING RESULTS\(^{hh}\)

- Sensitizing EGFR mutation positive (see NSCL-18)
  - ALK positive (see NSCL-21)
  - ROS1 positive (see NSCL-24)
  - BRAF V600E positive (see NSCL-25)

- PD-L1 \(\geq 50\%\) and EGFR, ALK negative or unknown (see NSCL-26)
- EGFR, ALK, ROS1, BRAF negative or unknown, PD-L1 \(< 50\%\) or unknown (see NSCL-27)
  - Sensitizing EGFR mutation positive (see NSCL-18)
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BEST RECOMMENDATIONS TODAY

NCCN Guidelines Version 2.2019
Non-Small Cell Lung Cancer

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NCCN Guidelines Version 2.2019
Non-Small Cell Lung Cancer

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## Emerging Biomarkers to Identify Novel Therapies for Patients with Metastatic NSCLC

<table>
<thead>
<tr>
<th>Genetic Alteration (ie, Driver event)</th>
<th>Available Targeted Agents with Activity Against Driver Event in Lung Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-level MET amplification or MET exon 14 skipping mutation</td>
<td>Crizotinib&lt;sup&gt;1-5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
| RET rearrangements                    | Cabozantinib<sup>6,7</sup>  
Vandetanib<sup>8</sup> |
| ERBB2 (HER2) mutations                | Ado-trastuzumab emtansine<sup>9</sup> |
| Tumor mutational burden (TMB)<sup>*</sup> | Nivolumab + ipilimumab<sup>10</sup>  
Nivolumab<sup>11</sup> |

*TMB is an evolving biomarker that may be helpful in selecting patients for immunotherapy. There is no consensus on how to measure TMB.*
TARGETED THERAPY FOR ADVANCED OR METASTATIC DISEASE

**Monitoring During Initial Therapy**
- Response assessment after 2 cycles, then every 2–4 cycles with CT of known sites of disease with or without contrast or when clinically indicated.

**Monitoring During Subsequent Therapy**
- Response assessment with CT of known sites of disease with or without contrast every 6–12 weeks. Timing of CT scans within Guidelines parameters is a clinical decision.

**Sensitizing EGFR Mutation Positive**
- First-line therapy
  - Afatinib\(^1\)
  - Erlotinib\(^2\)
  - Dacomitinib\(^3\)
  - Gefitinib\(^4,5\)
  - Osimertinib\(^6\)
- Subsequent therapy
  - Osimertinib\(^7\)

**ALK Rearrangement Positive**
- First-line therapy
  - Alectinib\(^8,9\)
  - Brigatinib\(^10\)
  - Ceritinib\(^11\)
  - Crizotinib\(^12,13\)
- Subsequent therapy
  - Alectinib\(^14,15\)
  - Brigatinib\(^16\)
  - Ceritinib\(^17\)
  - Lorlatinib\(^18\)

**ROS1 Rearrangement Positive**
- First-line therapy
  - Ceritinib\(^19\)
  - Crizotinib\(^20\)

**BRAF V600E Mutation Positive**
- First-line therapy
  - Dabrafenib/trametinib\(^21\)
- Subsequent therapy
  - Dabrafenib/trametinib\(^22,23\)

**PD-L1 ≥50%**
- First-line therapy\(^*\)
  - Pembrolizumab\(^24,25\)
  - (Carboplatin or cisplatin)/pemetrexed/pembrolizumab (non-squamous)\(^26\)
  - Carboplatin/paclitaxel/bevacizumab/atezolizumab (nonsquamous)\(^27\)
  - (Carboplatin or cisplatin)/(paclitaxel or albumin-bound paclitaxel)/pembrolizumab (squamous)\(^28\)
PD-L1 AND FIRST-LINE PEMBROLIZUMAB

Hazard ratio for disease progression or death, 0.50 (95% CI, 0.37–0.68)
P<0.001

<table>
<thead>
<tr>
<th>Month</th>
<th>No. at Risk Pembrolizumab</th>
<th>No. at Risk Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>154</td>
<td>151</td>
</tr>
<tr>
<td>3</td>
<td>104</td>
<td>99</td>
</tr>
<tr>
<td>6</td>
<td>89</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>15</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Reck, NEJM 2016
KEYTRUDA® (pembrolizumab) Monotherapy Met Primary Endpoint in Phase 3 KEYNOTE-042 Study, Significantly Improving OS as First-Line Therapy in Locally Advanced or Metastatic NSCLC Patients Expressing PD-L1 in at Least 1 Percent of Tumor Cells

Release Date:
Monday, April 9, 2018 6:45 am EDT
IMMUNOTHERAPY AND TMB

A Tumor PD-L1 Expression

PD-L1 Expression of ≥1%

Hazard ratio for disease progression or death, 0.62 (95% CI, 0.44–0.88)

No. at Risk

Nivolumab + ipilimumab

101 65 50 40 26 16 7 2 0

Chemotherapy

112 73 35 13 6 5 3 0 0

PD-L1 Expression of <1%

Hazard ratio for disease progression or death, 0.48 (95% CI, 0.27–0.83)

No. at Risk

Nivolumab + ipilimumab

38 20 16 15 10 8 4 1 0

Chemotherapy

48 30 16 4 1 1 1 0 0

B Tumor Histologic Type

Squamous

Hazard ratio for disease progression or death, 0.63 (95% CI, 0.39–1.04)

No. at Risk

Nivolumab + ipilimumab

44 26 17 14 9 6 3 2 0

Chemotherapy

56 33 13 2 1 0 0 0 0

Nonsquamous

Hazard ratio for disease progression or death, 0.55 (95% CI, 0.38–0.80)

No. at Risk

Nivolumab + ipilimumab

95 59 49 41 27 18 8 1 0

Chemotherapy

104 70 38 15 6 6 4 0 0

Hellman, NEJM 2018
MET EXON 14 AND CRIZOTINIB

73yoM never smoker
*MET* c.3028+1G>T

After 2 months on crizotinib

Drilon, ASCO 2016
FDA News Release

FDA approves first cancer treatment for any solid tumor with a specific genetic feature

For Immediate Release

May 23, 2017

Le, NEJM 2015
FDA approves larotrectinib for solid tumors with NTRK gene fusions

On November 26, 2018, the Food and Drug Administration granted accelerated approval to larotrectinib (VITRAKVI, Loxo Oncology Inc. and Bayer) for adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation, that are either metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory alternative treatments or whose cancer has progressed following treatment.

This is the second tissue-agnostic FDA approval for the treatment of cancer.

Approval was based on data from three multicenter, open-label, single-arm clinical trials: LOXO-TRK-14001 (NCT02122913), SCOUT (NCT02637687), and NAVIGATE (NCT02576431). Identification of positive NTRK gene fusion status was prospectively determined in local laboratories using next generation sequencing (NGS) or fluorescence in situ hybridization (FISH). NTRK gene fusions were inferred in three pediatric patients with infantile fibrosarcoma who had a documented ETV6 translocation by FISH. The major efficacy outcome measures were overall response rate (ORR) and response duration, as determined by a blinded independent review committee according to RECIST 1.1.
LAROTRECTINIB: NTRK FUSIONS

Drillon, NEJM 2018
RET, NSCLC, AND LOXO-292

Efficacy of LOXO-292 regardless of RET fusion partner

Drilon, Lancet Onc 2016
Testing in NSCLC is standard

Comprehensive NGS testing allows the best opportunity to obtain multiple answers in an expedited manner

Barriers to Testing Access and Coverage Must be Solved Globally
THANK YOU!

You may email questions to:

Octavia.vogel@cancer.org
UNDERSTANDING AND ADDRESSING GAPS IN TESTING

JENNIFER C. KING, PH.D.
LUNG CANCER ALLIANCE
CURRENT GUIDELINES: MOLECULAR TESTING/BIOMARKER TESTING

NCCN Guidelines Version 1.2019
Non-Small Cell Lung Cancer

CLINICAL PRESENTATION

Advanced or metastatic Disease

HISTOLOGIC SUBTYPE

• Establish histologic subtype with adequate tissue for molecular testing (consider rebiopsy if appropriate)
• Smoking cessation counseling
• Integrate palliative care (See NCCN Guidelines for Palliative Care)

Squamous cell carcinoma

Molecular testing

Testing should be conducted as part of broad molecular profiling

PD-L1 testing (category 1)

ALK positive (see NSCL-21)
ROS1 positive (see NSCL-24)
BRAF V600E positive (see NSCL-25)

EGFR, ALK, ROS1, BRAF negative or unknown, PD-L1 >50% or unknown (see NSCL-27)

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EGFR, ALK, ROS1, BRAF, negative or unknown, PD-L1 <50% or unknown (see NSCL-28)
MULTIPLE SINGLE GENE TESTS: AN EXAMPLE

Paraffin block: 37x24x9mm

Biopsy tissue – similar to a pencil lead refill

Single gene companion diagnostic: ~5 unstained slides

FOR ALL THE POTENTIAL COMPANION DIAGNOSTIC TESTS
FDA APPROVALS FOR PANEL NGS COMPANION DIAGNOSTICS

Oncomine Dx Target Test – Approved June 2017
- 23 genes
- NSCLC, multiple therapeutic indications

Foundation One CDx – Approved November 2017
- 324 genes
- Multiple cancer types, multiple therapeutic indications

https://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm
CMS COVERAGE DECISION

- Final CMS Decision Memo on March 16, 2018

**Decision Summary**

A. Coverage

The Centers for Medicare & Medicaid Services (CMS) has determined that Next Generation Sequencing (NGS) as a diagnostic laboratory test is reasonable and necessary and covered nationally, when performed in a CLIA-certified laboratory, when ordered by a treating physician and when all of the following requirements are met:

1. Patient has:
   a. either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
   b. either not been previously tested using the same NGS test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician; and
   c. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

2. The diagnostic laboratory test using NGS must have:
   a. FDA approval or clearance as a companion in vitro diagnostic; and
   b. an FDA approved or cleared indication for use in that patient’s cancer; and
   c. results provided to the treating physician for management of the patient using a report template to specify treatment options.

So broad panel testing is available and in some cases covered.... But is it happening?
AN EARLY CASE STUDY ON EGFR TESTING

Predictors of EGFR testing:
- Affiliation with an academic medical institute
- Participation in a NCI Cooperative Group
- Availability of PET or cardiothoracic surgery
- Metropolitan counties
- Above average education or income

Lynch et al. Genet Med 2013
Random sample of 1358 patients diagnosed in 2010 w/ NSCLC in SEER
Records abstracted, MD queried
EGFR testing occurred in 23% in Stage IV NS-NSCLC
Significant disparities were observed in testing by insurance status (Medicaid or none/unknown), comorbidity, ethnicity, and age
EGFR TESTING IN THE U.S. – MEDICARE CLAIMS

- Claims data reviewed from 2011-2013 for new diagnoses of lung cancer

- Aim to see if molecular testing performed for EGFR and/or KRAS

- Patient zip code had the greatest impact on odds to undergo testing
  - Patients in Boston referral region most likely to be tested (OR 4.94)

- Patient demographics also impacted odds to be tested
  - Asian/Pacific Islanders most likely to be tested (OR 1.63)
  - Minorities and Medicaid patients less likely to be tested (Medicaid OR 0.74)
  - Hispanics and African Americans less likely to be tested (OR 0.97, 0.95)

EGFR TESTING IN THE U.S. – MEDICARE CLAIMS

<table>
<thead>
<tr>
<th>Year diagnosed</th>
<th>Molecular test 83912</th>
<th>Claim for reporting a molecular test&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EGFR</td>
<td>KRAS</td>
<td>Multiple</td>
</tr>
<tr>
<td>2010</td>
<td>18,845</td>
<td>2,516</td>
<td>1,095</td>
</tr>
<tr>
<td>2011</td>
<td>12,254</td>
<td>1,235</td>
<td>655</td>
</tr>
<tr>
<td>2012</td>
<td>11,316</td>
<td>2,714</td>
<td>1,460</td>
</tr>
<tr>
<td>2013</td>
<td>–</td>
<td>12,433</td>
<td>4,856</td>
</tr>
<tr>
<td>Total</td>
<td>42,415</td>
<td>18,898</td>
<td>8,066</td>
</tr>
</tbody>
</table>

Percent of patients tested

<table>
<thead>
<tr>
<th>Years</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>Change 2011–2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients diagnosed with lung cancer</td>
<td>245,576</td>
<td>227,929</td>
<td>215,036</td>
<td>-12.4%</td>
</tr>
<tr>
<td>Patients who a claim for surgical pathology analysis&lt;sup&gt;c&lt;/sup&gt;</td>
<td>167,291</td>
<td>155,408</td>
<td>142,469</td>
<td>-14.8%</td>
</tr>
<tr>
<td>Patients who had a claim for a molecular test&lt;sup&gt;d&lt;/sup&gt;</td>
<td>13,008</td>
<td>13,818</td>
<td>13,259</td>
<td>1.9%</td>
</tr>
<tr>
<td>Percent of patients with tissue who were tested</td>
<td>7.78</td>
<td>8.89</td>
<td>9.31</td>
<td>19.7%</td>
</tr>
</tbody>
</table>
Genomic Profiling of Advanced NSCLC

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>814 (100)</td>
</tr>
<tr>
<td>Tested for <em>EGFR/ALK</em></td>
<td>479 (59)</td>
</tr>
<tr>
<td>Tested for all 7 NCCN recommended mutations</td>
<td>63 (8)</td>
</tr>
<tr>
<td>Patients aged ≥65 y</td>
<td>464 (100)</td>
</tr>
<tr>
<td>Tested for <em>EGFR/ALK</em></td>
<td>272 (59)</td>
</tr>
<tr>
<td>Tested for all 7 NCCN recommended mutations</td>
<td>31 (7)</td>
</tr>
</tbody>
</table>

Abbreviations: *ALK* = anaplastic lymphoma kinase; *EGFR* = epidermal growth factor receptor; NCCN = National Comprehensive Cancer Network.
“Community-based practices may face challenges in developing and implementing precision medicine programs in the following domains:

- molecular test selection
- timing of testing
- tissue collection
- interpretation of genomic results (actionability)
- genetic counseling and patient attitudes
- clinical trial eligibility
- financial concerns.”
Lung Cancer Alliance: From Jan 1, 2016 to July 31, 2017, of HelpLine callers asked if they had molecular testing, more than half (54%) said “No”

Bonnie J. Addario Lung Cancer Foundation: In a 2017 review, their Centers of Excellence were only testing 60% of patients with Stage III/IV lung cancer

2018 CancerCare roundtable and white paper with two calls to action:
- Patient advocacy groups, health care providers and industry need to align on common terminology and messaging with regard to biomarkers and other patient educational materials.
- A comprehensive physician survey is necessary in order to gain a fuller understanding of physicians’ knowledge gaps and other reasons to explain why biomarker testing is not being performed more frequently.
LUNGevity’s Take Aim Initiative is aimed at biomarker testing and ensuring that patients have access to comprehensive biomarker testing to help guide their treatment decisions in a timely way.

**Goal:**

All people diagnosed with lung cancer have comprehensive biomarker testing tested *at diagnosis* so they:

- Are given access to therapies or clinical trials which are targeted at their cancer’s mutations
- They have the information that they need to participate in treatment decision making

*Slide courtesy: LUNGevity Foundation*
TAKE AIM INITIATIVE OVERVIEW

**Changing Practice Behavior**
- Accreditations – Who? How?
- CME Requirements
- Guideline Adherence

**Pathology/Labs**
- Testing – Sequential vs NGS/IHC
- Tissue sparing
- Tissue handling
  - CAP/AMP

**Tissue Acquisition**
- Pulmonologists
- Interventional Radiologists
- Thoracic Surgeons

**Biomarker Testing**
- Patient Advocacy Groups
- Industry Partners

**Public Policy**
- CMS Reimbursement
- Private Payer Reimbursement
- 14-Day Rule
- QOPI Metrics

**Awareness/Education**

---

*Slide courtesy: LUNGevity Foundation*
Lung Cancer Alliance

Personalized Treatment and Trial Navigation Program

Biomarker Testing Component

• IRB Approved Registry Protocol
• Access to Genomic & Proteomic Testing (tissue or blood)
• Patients consent, physicians sign orders, both receive results
• Combined report with treatment recommendations, reviewed by an expert tumor board
• Lung Cancer Alliance Treatment Navigator to educate patient, provide free educational materials, explain choices and rationale, follow-up for other support

www.lungmatch.org  1-800-298-2436
The primary reasons why patients are not molecularly tested are consistent across centers; biopsy fail, or will not affect the treatment plan.

**Reasons Why Patients Are Not Molecularly Tested**

<table>
<thead>
<tr>
<th>Reason</th>
<th>COE (n = 8)*</th>
<th>Non-COE (n = 9)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy fail</td>
<td>38%</td>
<td>33%</td>
</tr>
<tr>
<td>Won’t change the treatment plan</td>
<td>38%</td>
<td>22%</td>
</tr>
<tr>
<td>Patient unfit for biopsy</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Patient has financial concerns about the test/procedure</td>
<td>83%</td>
<td>77%</td>
</tr>
<tr>
<td>Patient refusal</td>
<td>25%</td>
<td>11%</td>
</tr>
<tr>
<td>Patient has financial concerns about the potential treatment</td>
<td>0%</td>
<td>11%</td>
</tr>
<tr>
<td>Others</td>
<td>13%</td>
<td>11%</td>
</tr>
</tbody>
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% of centers

1. **1st most common**
2. **2nd most common**
3. **3rd most common**

Q2.130 was only asked to respondents who do use molecular testing in at least some of their patients. For those patients that are not molecularly tested, please rank the most common reasons why they are not tested from the list below.
LIQUID BIOPSY

Consider as an option for:

• Patients without evaluable tissue from initial biopsy or biopsy would cause significant delay

• Testing at progression
**AT PROGRESSION: IASLC RECOMMENDATION**

**Patient with NSCLC progressive or recurrent disease during treatment with TKI**

1. **Perform molecular analysis* on liquid biopsy (ctDNA)**
   - **Targetable resistance mutation absent**
     - **Feasible**
       - Perform molecular analysis* on tissue biopsy specimen #: NGS is preferred +; Treat with SOC therapy based on presence or absence of oncogenic driver; Perform PD-L1 IHC as needed
     - **Not Feasible**
       - Evaluate the potential benefit of other therapy for marker unknown or best supportive care
   - **Targetable resistance mutation present**
     - **Tissue re-biopsy**
     - **Treat with SOC therapy based on presence of oncogenic driver**

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* cobas/ddPCR for EGFR mutation
NGS preferred for ALK and ROS1

# Strongly suggest tissue sparing to facilitate participation in clinical trials

+ While NGS is preferred, based on availability, other validated assays are acceptable
LIQUID BIOPSY

Consider as an option for:

- Patients without evaluable tissue from initial biopsy or biopsy would cause significant delay
- Patients at progression
- “Can be considered at initial diagnosis” In parallel to tissue? Faster turnaround? Added value?
Clinical Implications of Plasma-Based Genotyping With the Delivery of Personalized Therapy in Metastatic Non-Small Cell Lung Cancer

Charu Aggarwal, MD, MPH; Jeffrey C. Thompson, MD; Taylor A. Black, BA; Sharyn I. Katz, MD, MTR; Ryan Fan, BA; Stephanie S. Yee, MS; Austin L. Chien, BA; Tracey L. Evans, MD; Joshua M. Bauml, MD; Evan W. Alley, MD, PhD; Christine A. Ciunci, MD, MSCE; Abigail T. Berman, MD, MSCE; Roger B. Cohen, MD; David B. Lieberman, MS, LCGC; Krishna S. Majmundar, BS; Samantha L. Savitch, BA; Jennifer J. D. Morrissette, PhD; Wei-Ting Hwang, PhD; Kojo S. J. Elenitoba-Johnson, MD; Corey J. Langer, MD; Erica L. Carpenter, MBA, PhD

Figure 3. Response of Patients to Plasma-Indicated Targeted Therapy as Measured by Response Evaluation Criteria in Solid Tumors (RECIST)

Waterfall plot shows the percentage change in target lesion diameter as determined by RECIST for patients with therapeutically targetable mutations detected by plasma. Forty-two patients with driver or resistance mutations underwent analysis, including 21 undergoing plasma next-generation sequencing at diagnosis and 21 at disease progression. Thirty-six patients (85.7%) achieved a complete response, partial response, or stable disease. An increase in size of target lesions by more than 20% indicates progressive disease, while decrease in size of target lesion of more than 30% indicates disease response.

And accompanying editorial: Guyawali & West
LIQUID BIOPSY

Also consider patient factors & reaching the unreachable
Guidelines recommend broad panel testing

There are FDA-approved and CMS-covered panel tests (although financial challenges & coverage issues remain)

Both researchers and the advocacy community has recognized under-testing and testing disparities & there are programs and projects aimed at addressing these gaps in care

Liquid biopsy may also be an option – particularly when tissue is not available
THANK YOU!

You may email questions to:

JKing@LungCancerAlliance.org
CASE PRESENTATION

DAVID SPIGEL, MD
Mr. WL is a 59 yo otherwise healthy active gentleman – works full-time and exercises regularly. Has never smoked.

Presents with a persistent cough (no dyspnea, hemoptysis, wt loss, or pain)

CT chest: 2cm RLL lesion and hilar node
PET: Uptake in the RLL and hilar lesions. Uptake also in a left iliac crest

What would be the next diagnostic test?
Navigation bronchoscopy: Adenocarcinoma in the RLL, Level 7 and 10R nodes.

**Next options in care:**

1. Start systemic therapy (carboplatin/pemetrexed/pembrolizumab)
2. Test for *EGFR, ALK, PD-L1*, await results
3. Test for NCCN markers, await results
4. Perform Comprehensive NGS Testing, await results
5. Biopsy the iliac crest
CASE: WL

Local EGFR, ALK, ROS, BRAF, MET, PD-L1 testing performed
Sample sent for Comprehensive NGS testing
Biopsy performed of the L-iliac crest

- Local testing: negative (PD-L1 low) – but report noted:
  *FISH for ALK failed to hybridize*
- *Iliac crest biopsy: Adenocarcinoma*
- *Comprehensive NGS: EML$-ALK Fusion identified*

- Alecitnib started
 QUESTIONS FOR GROUP DISCUSSION

- Do any participants have similar cases they would like to discuss?
- What are the biggest challenges faced by your cancer centers related to molecular testing and immunotherapies for lung cancer patients?
- Any strategies for managing challenges?
LUNG CANCER ECHO IMPLEMENTATION GRANT PROGRAM

- **Purpose/Goal:** A small grant program to assist cancer centers participating in the Lung Cancer ECHO in implementing lessons learned from the ECHO sessions with the goal of enhancing the level of care provided to lung cancer patients.

- **Simplified and expedited grant application process**

- **Application Deadlines:** Mini grant applications must be submitted by Friday, December 21, 2018 to the Office of Sponsored Programs, American Cancer Society at spo@cancer.org.

- **Notification:** Applicants will be notified if their application is approved by January 11, 2019. Once applications are approved, the funding will be distributed by January 31, 2019.
POTENTIAL PROJECT IDEAS

- **Topic areas (Others can be proposed)**
  - Reducing transportation costs for lung cancer patients to receive treatment at other facilities (i.e. surgery) or to participate in clinical trials
  - Initiation of a medical neighborhood that includes partners across the continuum of care to ensure coordinated patient care
  - Efforts to provide continuing education to providers related to lung cancer diagnosis, staging, and treatment
  - Support for on-site tobacco cessation for patients diagnosed with lung cancer (ACS is interested in piloting its group tobacco cessation program Fresh Start with patients)
  - Changes to internal systems, processes, EHRs, etc. to improve the quality of care provided to lung cancer patients (guideline adherence)
  - Improving efforts to deliver survivorship care plans/care transition meetings and provide at least one follow up with patients receiving the plans.
  - Efforts to empower patients in shared decision making related to their treatment and care
- **Project Timeline:** The 6-month project will start on February 1, 2019 and conclude on July 1, 2019. (We may consider short extensions if needed to maximize program reach)

- **Reporting Requirements:** Awardees will be required to submit a brief final progress and financial report on Friday, August 30, 2019. A template will be provided.

- **Funding Amount:** $10,000 (No indirect)

- **Eligibility:** Participating Cancer Centers who have attended at least 3 ECHO sessions to date through November and who can commit to attending at least 3 additional sessions before the end of the clinic in May.

- **Interested/Questions:** Contact Octavia Vogel at Octavia.vogel@cancer.org
JOIN US FOR LUNG CANCER PATIENT SUPPORT ECHO SESSION 8

LUNG CANCER TREATMENT:
OVERVIEW OF COMMON AND NEW TREATMENTS, LONG-TERM PROGNOSIS, AND SUPPORTING PATIENTS IN MAKING INFORMED TREATMENT DECISIONS

FACILITATOR:
DR. KEVIN OEFFINGER, MD
JANUARY TBD
9:00 AM ET

Presenters:

Jim Jett, M.D.
Professor of Medicine
Department of Oncology
National Jewish Health System

David Spigel, M.D.
Chief Scientific Officer
Director, Lung Cancer Research Program
Sarah Cannon Health System