NCCN Non-Small Cell Lung Cancer Panel Perspective
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Disclosures

For research that I conduct, my institution receives funding from:

• Roche
• Takeda
• Novartis
• Mirati
• Pfizer
Disclaimer

I am not a representative of the NCCN.
I am merely a member of one of the guidelines panels.
NCCN Clinical Practice Guidelines

• Minimize variation in care to improve outcomes and avoid unnecessary treatments
• Provide standards for quality of care assessment and improvement strategies
• Educational instruments
• Basis for coverage determination by CMS and most major payers
NCCN Clinical Practice Guidelines

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• Provide standards for quality of care assessment and improvement strategies

• Educational instruments

• Basis for coverage determination by CMS and most major payers
NCCN Guidelines Downloads

Non-Small Cell Lung Cancer

• 2017 – 460,530
• 2018 – 569,960
• Increase – 24%
NCCN Guidelines for Patients

Lung Cancer
Early and Locally Advanced

Available online at NCCN.org/patients

Lung Cancer
Metastatic

Available online at NCCN.org/patients

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What we think about testing for...

**Mutations/Gene Fusions (by NGS):**
- KRAS-G12C: 12%
- KRAS-nonG12C: 16%
- EGFR sensitizing: 24%
- EGFR exon 20 ins: 16%
- ALK: 3%
- ROS1: 2%
- BRAF: 1%
- Met exon 14: 3%
- ERBB2 (HER2): 2%
- RET: 2%
- NTRK: 0%
- Unknown driver: 33%

**PD-L1 (by IHC):**
- PD-L1 ≥50%: 15%
- PD-L1 1-49%: 18%
- PD-L1 negative: 67%

MSKCC data, June 2019
What we think about testing for...

This is **11 different things** to test, using at least two (and often more) approaches, some have approved drugs, some don’t.
Testing is key part of initial evaluation

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
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<tbody>
<tr>
<td>Advanced or metastatic disease</td>
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<tr>
<td>• Establish histologic subtype(a) with adequate tissue for molecular testing (consider rebiopsy(i) if appropriate)</td>
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<tr>
<td>• Smoking cessation counseling</td>
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<tr>
<td>• Integrate palliative care(c) (See <a href="#">NCCN Guidelines for Palliative Care</a>)</td>
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<table>
<thead>
<tr>
<th>Histologic Subtype(a)</th>
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<tbody>
<tr>
<td>• Adenocarcinoma</td>
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<tr>
<td>• Large cell</td>
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<tr>
<td>• NSCLC not otherwise specified (NOS)</td>
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<table>
<thead>
<tr>
<th>Testing(ii)</th>
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<tbody>
<tr>
<td>• Molecular testing</td>
</tr>
<tr>
<td>▶ <em>EGFR</em> mutation testing (category 1)</td>
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<tr>
<td>▶ <em>ALK</em> testing (category 1)</td>
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<tr>
<td>▶ <em>ROS1</em> testing</td>
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<tr>
<td>▶ <em>BRAF</em> testing</td>
</tr>
<tr>
<td>▶ Testing should be conducted as part of broad molecular profiling(kk,ii)</td>
</tr>
<tr>
<td>▶ PD-L1 testing (category 1)</td>
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\(kk\) The NCCN NSCLC Guidelines Panel strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC. See [Emerging Biomarkers to Identify Patients for Therapies (NSCLC-H)](#).

\(ii\) Testing should include the neurotrophic receptor kinase (NTRK) gene fusion; if positive, see [NSCL-27](#).
Testing is key part of initial evaluation.

The NCCN NSCLC Guidelines Panel strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC. See Emerging Biomarkers to Identify Patients for Therapies (NSCL-H).

Testing should include the neurtrophin receptor kinase (NTRK) gene fusion; if positive, see NSCL-27.
**NCCN Guidelines Version 1.2020**

**Non-Small Cell Lung Cancer**

### Clinical Presentation

- 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)

### Histologic Subtype

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

### Testing

#### 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

- **PD-L1 testing (category 1)**

#### Consider EGFR mutation and ALK testing in never smokers or small biopsy specimens, or mixed histology

### Testing Results

- **Sensitizing EGFR mutation positive** (see NSCL-19)
- **ALK positive** (see NSCL-22)
- **ROS1 positive** (see NSCL-25)
- **BRAF V600E positive** (see NSCL-26)
- **PD-L1 ≥1% and EGFR, ALK, ROS1, BRAF, negative** (see NSCL-28)
- **EGFR, ALK, ROS1, BRAF negative PD-L1 <1%** (see NSCL-30)

- **Sensitizing EGFR mutation positive** (see NSCL-19)
- **ALK positive** (see NSCL-22)
- **ROS1 positive** (see NSCL-25)
- **BRAF V600E positive** (see NSCL-26)
- **PD-L1 ≥1% and EGFR, ALK, ROS1, BRAF, negative** (see NSCL-28)
- **EGFR, ALK, ROS1, BRAF, negative PD-L1 <1%** (see NSCL-31)
Crizotinib in Patients with Metastatic NSCLC with MET exon 14 alterations

Biomarker Data Key

- **MET exon 14 alteration region**
- **MET exon 14 alteration type**
- **MET amp status**

- Splice donor
- Splice acceptor
- Canonical
- Not detected

Drilon et al WCLC 2018
## 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>
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<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>
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</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)* | Nivolumab + ipilimumab<sup>10</sup>  
Nivolumab<sup>11</sup> |
Without approved drugs, many newer targets which would lead to clinical trials are not in the guidelines.

Efficacy of Selpercatinib: Primary Analysis Set (n=105)

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<thead>
<tr>
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<th>Overall (n=105)</th>
<th>CNS** (n=11)</th>
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<tbody>
<tr>
<td><strong>ORR (95% CI)</strong></td>
<td>68% (58%–76%)*</td>
<td>91% (59%–100%)</td>
</tr>
<tr>
<td>CR</td>
<td>2%</td>
<td>18%</td>
</tr>
<tr>
<td>PR</td>
<td>66%</td>
<td>73%</td>
</tr>
<tr>
<td>SD</td>
<td>26%</td>
<td>9%</td>
</tr>
<tr>
<td>PD</td>
<td>2%</td>
<td>-</td>
</tr>
<tr>
<td>NE</td>
<td>5%</td>
<td>-</td>
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</table>

Note: * indicates **p < 0.05, ** indicates **p < 0.01; † indicates non-sustained effect at end of study, and ‡ indicates improvement in study by the investigator. CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, NE = no evaluation. DCD = dose decreased or delayed; ** indicates **p < 0.01; † indicates non-sustained effect at end of study, and ‡ indicates improvement in study by the investigator. CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, NE = no evaluation. DCD = dose decreased or delayed; DCR = durable complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = no evaluation.
Without approved drugs, many newer targets which would lead to clinical trials are not in the guidelines.

Some targets which are likely to have approved drugs:
- RET
- EGFR exon 20 insertions
- KRAS G12C
Conclusions

• The guidelines aim to educate the multidisciplinary care team and patients about molecular testing

• The guidelines approach each molecular target and the relevant drugs and guide physicians based on the data supporting drug efficacy