Bridging the Gaps in Precision Oncology: Opportunities in Non-Small Cell Lung Cancer

FINDINGS FROM THE AMCP MARKET INSIGHTS PROGRAM

Meeting Objectives

- Provide a foundational understanding of the NSCLC patient journey from patient identification to patient selection and management.
- Share insights on how effective referral, utilization management, and advanced diagnostics can improve patient outcomes and reduce costs.
- Identify the barriers that impede evidence-based and quality care throughout the NSCLC patient journey.

Introduction

Lung cancer is the most common cancer worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of all lung cancers. The National Institutes of Health estimated that cancer care cost the US $208.9 billion in 2020, $23.8 billion of which was due to lung cancer.1 The treatment of NSCLC lung cancer has advanced significantly based on the use of genomic testing to target the best therapeutic treatment. Genetic biomarkers are used for early detection and prognosis, to inform treatment options, and to guide the development of targeted therapies that have improved outcomes for patients. For health plans and payer stakeholders, precision oncology provides a long-anticipated strategy to control costs, utilization, and product waste in cancer care. However, realizing these benefits is subject to overcoming barriers impacting the timeliness of care for patients with NSCLC. Today the optimal patient journey is impeded by barriers such as operational inefficiencies, limited understanding of biomarker strategies, inappropriate test result usage, and access barriers. The use of biomarker-based targeted therapies is expected to continue to grow with most clinical trials for oncology therapies utilizing biomarkers to identify patient populations for treatment. To understand the appropriate and cost-effective use of biomarker-driven treatment selection in NSCLC, AMCP convened an expert panel of managed care stakeholders. Panelists included representatives from national and regional health plans, integrated delivery systems, laboratories, pharmacy benefit managers,
CLINICAL SPOTLIGHT
Evolution of NSCLC Treatments

Historically platinum based doublet chemotherapy was used in the 1st line setting in patients with NSCLC with good performance, providing an overall response rate of approximately 25%, median progression free survival of 4–6 months and overall survival of 8–10 months. Although chemotherapy can extend survival, it is not curative in patients with advanced disease, and many patients experience significant toxicity from chemotherapy including severe leukopenia, vomiting, and neurotoxicity.4,6

In recent years, the treatment of NSCLC has changed based on the determination of driver mutations in tumors and the progression-free survival has more than doubled for patients with specific mutations.7,8

Similarly, immunotherapy aimed at altering checkpoint inhibition through the programmed death ligand 1 (PD-L1) has shown an improvement in overall survival and significantly reduced adverse events compared to chemotherapy for patients with high PD-L1 expression.9

CLINICAL SPOTLIGHT
Significance of Liquid Biopsy

Blood-based tests continue to gain traction as an alternative to traditional solid tissue biopsy-based diagnostic tests for cancer. These tests allow oncologists to screen patients for the presence of cancer biomarkers from a blood sample in some cases where a tumor biopsy cannot be obtained or where there is not enough high-quality tissue to be used for genetic testing. Liquid biopsies also allow for multiple samples to be taken over time, which may help providers understand what kind of genetic or molecular changes are taking place in a tumor.16

In recent years, the treatment of NSCLC has changed based on the determination of driver mutations in tumors and the progression-free survival has more than doubled for patients with specific mutations.7,8

Similarly, immunotherapy aimed at altering checkpoint inhibition through the programmed death ligand 1 (PD-L1) has shown an improvement in overall survival and significantly reduced adverse events compared to chemotherapy for patients with high PD-L1 expression.9

Figure 1. Participant Demographics

and the patient journey (Figure 2). Testing of lung cancer specimens for these alterations is important for identification of potentially efficacious targeted therapies, to avoid use of therapies unlikely to provide clinical benefit, and to reduce adverse events.2,3

Currently, several testing strategies are available to identify genomic alterations in NSCLC. Testing can be conducted as sequential testing of single genes, hotspot panel testing for a handful of common genomic alterations, or broad-based testing. Running
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Figure 2. NSCLC Patient Journey Through Biomarker Analysis

**HEALTHCARE TEAM**

Primary care doctors are often the first to suspect or find cancer. They work together with the other members of the healthcare team to coordinate cancer care.

**BIOMARKER TESTING**

Numerous gene alterations have been identified that impact therapy selection in NSCLC. Testing of lung cancer specimens for these alterations is important for identification of potentially efficacious targeted therapies, as well as avoidance of therapies unlikely to provide clinical benefit.

Liquid assays are noninvasive, fast, and easily repeatable over time, but they may be less sensitive than tissue-based assays and therefore cannot serve as stand-alone testing for patients with NSCLC. Sometimes additional biopsies (either tissue or liquid) are recommended.

Next-generation sequencing (NGS) is a technology for determining the sequence of DNA or RNA to study genetic variation associated with diseases. Broad-based genomic testing approaches that efficiently utilize limited biopsy tissue are most commonly NGS-based.

**BIOMARKER DRIVEN TREATMENT SELECTION**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>ALK</td>
</tr>
<tr>
<td>KRAS</td>
<td>ROS1</td>
</tr>
<tr>
<td>NTRK1/2/3</td>
<td>RET</td>
</tr>
<tr>
<td>PD1</td>
<td></td>
</tr>
</tbody>
</table>

**GENES**

- ALK: anaplastic lymphoma kinase
- BRAF: B-Raf proto-oncogene
- EGFR: Epidermal Growth Factor Receptor
- ERBB2: Erb-B2 Receptor Tyrosine Kinase
- KRAS: KRAS proto-oncogene
- METex14: mesenchymal-epithelial transition exon 14
- NTRK: neurotrophic tyrosine receptor kinase
- PD-L1: programmed death ligand 1
- RET: rearranged during transfection
- ROS1: ROS proto-oncogene 1

**TUMOR DNA TESTING**

- ERBB2/HER2
- METex14
- ROS1

**PLASMA/CELL-FREE DNA TESTING**

- Plasma Cell-Free/Circulating Tumor DNA Testing
a sequence of single-gene tests can be more time consuming and may require a large tissue sample, which may not be available if NSCLC is detected at an advanced stage. As a result, one or more re-biopsies may be needed to complete the sequence, which can delay treatment, add costs, and cause inconvenience and discomfort to patients. Broad-based genomic testing utilizes limited biopsy tissue while maximizing diagnostic genomic information and is commonly done with next-generation sequencing (NGS). NGS is a strategy to simultaneously test for multiple alterations using a single tissue sample. Results from broad biomarker testing can also identify opportunities for enrollment in clinical trials and future or second-line treatment options.

In NSCLC, more than 70% of patients have tumors with biomarker alterations related to therapeutic treatment options. Despite guideline recommendations for testing (Table 1) and an expanding body of evidence supporting the clinical value of genomic testing, it remains underutilized with up to 64% of patients with advanced NSCLC not receiving personalized treatment. Patients are lost at various steps along the precision oncology pathway due to operational inefficiencies, limited understanding of biomarker strategies, inappropriate test result usage, and access barriers.

In the US, several therapies that target specific alterations have been approved by the US Food and Drug Administration (FDA) and are recommended by the American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), and National Comprehensive Cancer Network (NCCN) (Table 2). FDA-approved NSCLC therapies are linked to two general biomarker categories: the presence of genetic driver mutations and the levels of PD-L1.

The expert panelists agreed that the future of cancer therapy lies in matching treatment to each patient’s genomic drivers but ranked the current realization of the benefits from biomarker-driven precision oncology in NSCLC as poor-to-average. The panelists stated that this ranking was mostly due to poor implementation across the fragmented US health care system and disparate reimbursement for genomic testing, and that the science behind biomarker-driven precision oncology was considered excellent.

**Framework for Improving Personalized Medicine in NSCLC**

The success of precision oncology in NSCLC relies on the accurate identification of patients with biomarker alterations as determined by laboratory testing and is subsequently used to guide therapeutic decisions. Panelists discussed the known clinical practice gaps along the precision NSCLC treatment pathway and identified opportunities for health plans to build a framework for improving biomarker-driven care of patients with NSCLC.

**Biomarker Test Ordering**

**GAP: Appropriate Testing was not Ordered or Treatment Began Before Testing was Ordered**

Data suggests that approximately 17.5% of patients with advanced NSCLC do not have any biomarker testing ordered, and 3.2% of patients receive

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Table 1. Strongly Advised NCCN Biomarker Tests in NSCLC

<table>
<thead>
<tr>
<th>Biomarker Test</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK rearrangement positive</td>
<td></td>
</tr>
<tr>
<td>BRAF V600E mutation positive</td>
<td></td>
</tr>
<tr>
<td>EGFR exon 19 deletion or exon 21 L858R mutation positive</td>
<td></td>
</tr>
<tr>
<td>EGFR exon 20 insertion mutation positive</td>
<td></td>
</tr>
<tr>
<td>EGFR S768I, L861Q, and/or G719X mutation positive</td>
<td></td>
</tr>
<tr>
<td>ERBB2 (HER2) mutation positive</td>
<td></td>
</tr>
<tr>
<td>KRAS G12C mutation positive</td>
<td></td>
</tr>
<tr>
<td>METex14 skipping mutation positive</td>
<td></td>
</tr>
<tr>
<td>NTRK1/2/3 gene fusion positive</td>
<td></td>
</tr>
<tr>
<td>PD-L1 &lt;1% and negative for actionable molecular biomarkers above</td>
<td></td>
</tr>
<tr>
<td>PD-L1 ≥1% and negative for actionable molecular biomarkers above</td>
<td></td>
</tr>
<tr>
<td>RET rearrangement positive</td>
<td></td>
</tr>
<tr>
<td>ROS1 rearrangement positive</td>
<td></td>
</tr>
</tbody>
</table>


Many barriers can affect test ordering for patients. The provider panelists noted some oncologists may not be aware of the testing recommendations, given the challenge of keeping up with the rapid advancements of cancer treatments and updates to treatment guidelines. Additionally, providers may not know which biomarker tests are covered by different insurers or which laboratory to use based on payer policies. Providers may also be influenced by factors around patient cost sharing.

“As a community oncologist when you are treating everything, and not just lung cancer, it is really hard to stay up to date on the latest advances.”

– Oncologist

The payer panelists echoed provider challenges around keeping up with the rapid advancements and growing complexity of cancer care and are looking for evidence to support treatment sequencing in NSCLC. There remains skepticism among some payers that broad-based biomarker testing meets a clinical utility threshold, and they are interested in engaging with oncologists to identify external measures of quality around appropriate biomarker testing. These issues underscore another concern that the wider use of broad-based NGS across solid tumors would create new opportunities for the use of off-label targeted therapies in routine cancer care. However, multigene panel–based assays are recommended if more than one biomarker-linked therapy is approved for the patient’s disease.3,17

Panelists also shared that targeted panels vary in their ability to capture all NCCN recommended biomarkers. One of the participants described an unpublished analysis where they found that only 2 of 32 NGS panels captured all the biomarkers and few

### Table 2. Select Molecular and Biomarker-Directed Therapy for Advanced or Metastatic NSCLC

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Frequency in NSCLC</th>
<th>First-line therapy</th>
<th>Subsequent therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR exon 19 deletion or exon 21 L858R</td>
<td>15-25%</td>
<td>Afatinib, Erlotinib, Dacomitinib, Gefitinib, Osimertinib, Erlotinib + bevacizumab (nonsquamous)</td>
<td>Osimertinib</td>
</tr>
<tr>
<td>EGFR S768I, LB61Q, G719X</td>
<td>1-2%</td>
<td>Afatinib, Erlotinib, Dacomitinib, Gefitinib, Osimertinib</td>
<td>Osimertinib</td>
</tr>
<tr>
<td>EGFR exon 20 insertion</td>
<td>4%</td>
<td>x</td>
<td>Amivantamab-vmjw, Mobocertinib</td>
</tr>
<tr>
<td>KRAS G12C</td>
<td>13%</td>
<td>x</td>
<td>Sotorasib, Adagrasib</td>
</tr>
<tr>
<td>ALK rearrangement</td>
<td>5%</td>
<td>Alectinib, Brigatinib, Ceritinib, Crizotinib, Lorlatinib</td>
<td>Alectinib, Brigatinib, Ceritinib, Lorlatinin</td>
</tr>
<tr>
<td>ROS1 rearrangement</td>
<td>2%</td>
<td>Ceritinib, Crizotinib, Entrectinib</td>
<td>Lorlatinib, Entrectinib</td>
</tr>
<tr>
<td>BRAF V600E</td>
<td>2%</td>
<td>Dabrafenib/trametinib, Dabrafenib, Vemurafenib</td>
<td>Dabrafenib/trametinib</td>
</tr>
<tr>
<td>NTRK 1/2/3 gene fusion</td>
<td>&lt;1%</td>
<td>Larotrectinib, Entrectinib</td>
<td>Larotrectinib, Entrectinib</td>
</tr>
<tr>
<td>MET exon 14 skipping mutation</td>
<td>3%</td>
<td>Capmatinib, Tepotinib, Crizotinib</td>
<td>Capmatinib, Tepotinib, Crizotinib</td>
</tr>
<tr>
<td>RET rearrangement</td>
<td>2%</td>
<td>Selpercatinib, Pralsetinib, Cabozantinib</td>
<td>Selpercatinib, Pralsetinib, Cabozantinib</td>
</tr>
<tr>
<td>ERBB2 (HER2) mutation</td>
<td>2%</td>
<td>x</td>
<td>Fam-trastuzumab deruxtecan-nxki, Ado-trastuzumab emtansine</td>
</tr>
</tbody>
</table>

As of February 2023
captured relevant biomarkers to determine clinical trial eligibility.\textsuperscript{18}

Proposed solutions to improve the process of ordering of biomarker testing include disease-specific algorithms to help select appropriate biomarker tests, up-to-date professional practice guidelines, and reflex broad-based biomarker testing. It was identified that community oncologists may benefit from having a simplified (e.g., 1 broad-based test regardless of cancer type) biomarker test that is also covered by insurance. Improvement in information technology, use of artificial intelligence to support clinical decision support systems, and quick access to laboratory consultations may also reduce gaps in ordering appropriate testing. Whenever it is indicated for actionable clinical decisions, conducting comprehensive biomarker testing early in the care of patients can better guide cancer treatment selection throughout the patient journey.

**Biomarker Testing Performance**

**GAP: Biomarker Testing Provided Inconclusive Results**

Estimates suggest that 14.5% of patients with advanced NSCLC who received biomarker testing will have an uninformative or inconclusive test result.\textsuperscript{11} NCCN recommends NSCLC biomarker testing be performed via a broad, panel-based approach, most typically performed by NGS. Most panelists agreed that NSCLC has an adequate number of actionable biomarkers for payers to cover NGS broad-based genomic testing approaches. Broad molecular profiling is currently defined by NCCN as molecular testing that identifies all biomarkers identified listed in Table 1.\textsuperscript{3}

Payers can provide consistent evidence-based coverage and value-based reimbursement of broad-based biomarker testing for appropriate cancers, including NSCLC, to efficiently use limited biopsy tissue while maximizing diagnostic genomic information. NGS also may help to avoid potentially missed targeted therapy options and improve testing uptake for newly approved biomarkers.

“We do not want to pay for something the oncologists are not going to use in treating the patient, and this is one concern around expanding broad-based biomarker testing.” – PBM

**Biomarker Testing Result Reporting**

**GAP: Turnaround Time Delays and Treatments Started without Consideration of Test Results**

Of the patients with advanced NSCLC receiving biomarker testing results, it is estimated that 4% will experience laboratory turnaround time delays that could lead to treatment decisions that do not take into consideration the testing results.\textsuperscript{11} Several barriers to NSCLC biomarker testing were discussed by the panelists. Operational barriers resulting from biomarker testing include the timeliness of result reporting, which can take more than 2 weeks, and the complexity of interpreting the results reports, which vary considerably across different laboratories.

Panelists shared that different testing platforms are associated with different turnaround times, and that NGS testing was associated with the quickest reporting time of around 2 weeks, which is supported by published evidence.\textsuperscript{19,20} The prolonged turnaround times from sequential single gene testing to NGS is important in advanced NSCLC, where the speed of test result may be crucial to a patient’s survival and quality of life. Liquid biopsies also add to the speed of tumor profiling, with the additional benefit of sampling being relatively painless to the patient.

Laboratory result reports vary based on the lab running the biomarker testing and there may be differences with respect to the level of detail included and the format of the results (e.g., PDF), which can
impact integration into electronic medical records (EMRs).

Both payers and providers described issues in interpreting the information in different laboratory reports. Biomarker summary reports (Table 3) may only list the biomarkers that tested positive or may also list the variant. This important clinical information may be listed next to the biomarker in the summary table, in a separate variants table (Table 4), or in the text section of the report.

Panelists noted the potential for accidental oversight when interpreting test results given the reporting delays, lack of integration into EMRs, and the variability and complexity of interpreting biomarker reports. A proposed solution to improve the interpretation of biomarker tests is to create standard formats that allow for easy importing of results into EMRs where the information can be incorporated into the clinicians workflow.

### Table 3. Example Biomarker Results Summary

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Method</th>
<th>Analyte</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK</td>
<td>NGS</td>
<td>RNA-Tumor</td>
<td>Fusion detected</td>
</tr>
<tr>
<td></td>
<td>IHC</td>
<td>Protein</td>
<td>Positive, 3+, 100%</td>
</tr>
<tr>
<td>BRAF</td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Pathogenic variation exon 25, p.G1269A</td>
</tr>
<tr>
<td>EGFR</td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Mutation not detected</td>
</tr>
<tr>
<td>ROS1</td>
<td>NGS</td>
<td>RNA-Tumor</td>
<td>Fusion not detected</td>
</tr>
<tr>
<td>PD-L1</td>
<td>IHC</td>
<td>Protein</td>
<td>Positive, high expression, TPS 50%</td>
</tr>
</tbody>
</table>

IHC: immunohistochemistry; TPS: tumor proportion score

### Table 4. Example Biomarker Variates Summary

<table>
<thead>
<tr>
<th>GENE</th>
<th>Method</th>
<th>Analyte</th>
<th>Interpretation</th>
<th>Protein Alteration</th>
<th>Exon</th>
<th>DNA Alteration</th>
<th>Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK</td>
<td>NGS</td>
<td>RNA-Tumor</td>
<td>Fusion detected</td>
<td>EML4-ALK</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Pathogenic variant</td>
<td>p.G1269A</td>
<td>25</td>
<td>c.3806G&gt;C</td>
<td>9</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Variant of uncertain significance</td>
<td>p.E119K</td>
<td>2</td>
<td>c.355g&gt;A</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Likely pathogenic variant</td>
<td>p.R87L</td>
<td>2</td>
<td>c.260G&gt;T</td>
<td>26</td>
</tr>
<tr>
<td>KIT</td>
<td>NGS</td>
<td>DNA-Tumor</td>
<td>Variant of uncertain significance</td>
<td>p.V853I</td>
<td>18</td>
<td>c.2554G&gt;A</td>
<td>50</td>
</tr>
</tbody>
</table>

### Treatment Decision

**GAP: Targeted Treatment was not Selected Despite Positive Biomarker Testing Results**

It is estimated that 29% of patients with NSCLC who undergo biomarker testing and receive results do not get appropriate targeted treatment. Unmatched treatment after detection of an actionable mutation may occur for various reasons. The panelists identified several factors that can impact patients with NSCLC receiving targeted therapies, such as a lack FDA-approved indication, lack of awareness of targeted treatment options, and comorbidities or treatment contraindications.

Providers may feel pressure to start therapy early and not wait for testing results. However, biomarker results should be interpreted before first-line treatment initiation, and several expert panelists reported using the NCCN guideline recommendation...
of holding immunotherapy for the first cycle and using platinum-doublet chemotherapy alone for patients with NSCLC needing urgent treatment while biomarker results are pending. A practice akin to hospital antibiotic stewardship programs where improved clinical outcomes and reduced harm is achieved by improving informed and targeted prescribing practices. Evidence suggesting that many patients with advanced NSCLC would not likely experience significant disease progression within the first 4 weeks of diagnosis may also reassure patients and providers to wait for testing results. Additionally, some targeted therapies can cause severe hepatotoxicity for patients when used after immunotherapy, which underlines the importance of selecting treatment that take into consideration treatment sequencing and side effects.

The fragmentation of the US health care system was identified as a major factor impacting biomarker-driven treatment. Employers and other plan sponsors have the option of carving in or carving out their pharmacy benefit program from their medical benefits. In this era of ultra-high-cost drugs, one way to manage costs and improve transparency is through integrated benefits that support the use of safe and cost-effective treatments. The lack of integration of insurance benefits and care delivery systems were both identified as potential barriers to implementing programs that improve the quality and safety of cancer care. One example of how benefits can impact patient care is when a health plan covers a biomarker test, but not its corresponding targeted treatment, or vice versa, when there is a prior authorization in place for a targeted therapy requiring a biomarker test result, but there is not coverage for the biomarker test.

Panelists mentioned that the upcoming Enhancing Oncology Model (EOM) from the Center for Medicare & Medicaid Innovation (CMMI) has the potential to reduce care fragmentation and improve the use of biomarker-driven precision oncology in NSCLC, since participating oncology practices will need to adhere to all nationally recognized clinical guidelines and offer coordinated care to their patients. Additionally, a possible role for pharmacy was identified to conduct a quality check that appropriate biomarker testing has been done for a patient before dispensing/administering a medication.

The panelists discussed the opportunity for payers to improve guideline-recommended biomarker testing in patients with NSCLC. Due to the potential of targeted therapies to increase toxicity for patients when used after immunotherapy and the underutilization of biomarker testing performed in accordance with the NCCN guidelines, both prior authorization and peer consultation were considered valuable tools payers could use to improve patient outcomes. Most of the payer experts reported that current prior authorizations require provider attestation of biomarker testing for coverage of NSCLC treatments, while others are using a proactive peer consultation model to improve adherence to recommended guidelines for molecular profiling (Figure 3). Engaging oncologists to conduct biomarker testing before beginning treatment selection better enables the use of first-line NSCLC therapies for each patient, resulting in better outcomes and improving the patient’s cancer care experience.

### Measuring Biomarker Testing

**GAP: Lack of Standardized Quality Measurement**

There is a great demand for accurate, useful information on health care quality that can inform the decisions of providers and payers. This is increasingly important as the health care system moves towards value-based reimbursement models. The panelists described a need for a biomarker quality measure that is evidence-based, consistent across different care delivery sites, and generates valuable information for both payers and providers. Ideally such a measure could also be used in value-based payment and
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Purchasing arrangements. One example raised as a possible guide to measuring appropriate biomarker-driven precision oncology is the work underway in Washington State — led by the Hutchinson Institute for Cancer Outcomes Research (HICOR) in collaboration with cancer care providers, health insurers, patients, and researchers — to develop a public report on the quality and cost of cancer care.\(^27\) The report promotes transparency by providing an analysis of quality measures linked to cost on selected indicators of care and includes a metric to measure adherence to treatment guidelines for NSCLC. The 2023 report will include a care quality measure on ordering biomarker testing.

“There is huge variation in realizing of the benefits, we really need quality measurement in an ongoing fashion to ascertain where we are in making progress with biomarker-driven precision oncology.”— Physician

Panel experts from pharmacy benefit managers (PBMs) and integrated delivery systems described how data from the EMR and administrative claims could be used to develop metrics for monitoring adherence to biomarker testing recommendations for NSCLC. Process measurement tools could include variables concerning diagnosis, molecular testing results, or provider attestation, and claims or EMR data on treatments received by a patient. Published data on the use/underuse of biomarker testing in NSCLC could be used as a benchmark.\(^{11,25}\)

**Measuring Cost Effectiveness**

**GAP: Precision Oncology does not Uniformly Benefit all Patients**

The high costs of new cancer treatments have threatened the affordability of cancer care. Oncologists and payers have experienced a shift in treatment paradigms from chemotherapy to targeted therapies. The high investment of precision oncology does not uniformly benefit all patients with cancer, making it critically important to consider the tradeoff between costs and health benefits.

The focus of discussions around cost-effectiveness of biomarker-driven treatment in NSCLC centered on different testing strategies — sequential testing of single genes compared to broad-based testing. Currently there is no standard broad-based comprehensive panel for NSCLC testing. Recommendations to conduct both tumor and liquid biopsies to improve the timeliness and biomarker results for patients with NSCLC were met with caution from the panelists around the cost-effectiveness of performing both tests for all patients. A proposed solution to address the affordability of this practice would be to bundle...
laboratory contracts to include both liquid and tumor biopsies under one value-based agreement.

“We need to also consider how expensive is it to not do the test, or to not act on the results of a test.”
— Integrated Delivery System

The panelists did not uniformly agree that biomarker testing currently helps prevent cycles of treatment trial and error in all patients with NSCLC. However, use of upfront NGS testing in patients with metastatic NSCLC has been associated with modest cost savings and shorter time-to-test results. Panelists did acknowledge the value of biomarker driven treatment selection in excess of the cost of the test itself and the value of identifying appropriate targeted therapy earlier in the patient journey. There is interest in understanding the total cost of care based on testing decisions (Figure 4), and the impact of treatment decisions on patient quality of life — including treatment side effects. Payers would also like to see published data around where savings from biomarker testing impacts the total cost of care equation (e.g., quality adjusted life years, health care resource utilization, use of secondary lines of therapy).

“What is the total cost of care if we test a group of individuals versus the total cost of care in a group of individuals that we would not test? That is the relatively simple question we need answered, but the answers are not out in the literature today.”
— Academia

Health Disparities

GAP: Significant Variability in Care Based on Ethnicity, SDOH, and Insurance

To increase interest in biomarker testing from payers and employers, the implementation of personalized oncology could be framed as an opportunity to reduce disparities and improve overall population health. Health care disparities refer to differences in health and health care between groups that stem from broader inequities. The distribution of smoking behavior within the US has changed over decades, and lung cancer has become more common among patients in lower socioeconomic groups. Among patients with NSCLC, there is significant variability in the prevalence of targetable genomic alterations according to genetic ancestry, histology, and smoking.
Patient-specific barriers include differences in rates of testing based on ethnicity and social determinates of health (SDOH), lack of ethnic diversity in clinical trials, and affordability and financial constraints. Factors effecting disparities in NSCLC care include regional variation, gender differences, and low-income status; this includes not all patients receiving appropriate biomarker testing. The failure to test appropriately not only causes harm by depriving access to life-prolonging targeted therapies, but also precludes access to clinical trials of targeted treatments.

When there is a health care tool that works, a disparity in the delivery of that tool is a quality problem. The opportunity to collaborate with the CMMI on outcome and quality measures related to disparities in precision oncology care could set a national standard, but panelists raised concerns with the length of time it takes to develop and implement national quality measures. Alternatively, internal process improvement measures could be pursued more quickly, and integrated health care systems were identified as likely partners in piloting quality-improvement efforts that focus on health equity in cancer care. It will also be important to have a champion within the organization who can bring cross functional teams together and to provide robust educational efforts to increase awareness of the value of precision oncology.

“Not every patient is getting standardized care and that is what we really want to know — that all care is equal.”
– Medicaid Health Plan

In the US, clinical outcomes and the source of insurance are strongly correlated. The panelists discussed the associations between insurance type, biomarker testing, and outcomes for patients with NSCLC. The Centers for Medicare & Medicaid Services (CMS) has issued a national coverage determination that increased access to comprehensive biomarker testing and NGS for Medicare beneficiaries. However, it was highlighted that Medicaid patients with NSCLC are less likely to receive recommended biomarker testing and targeted therapy. Inconsistent Medicaid coverage policies across states was suggested as a potential explanation for testing variation and that often the reimbursement for services is not adequate. Regardless of the reasons, these variations contribute to healthcare disparities among Medicaid beneficiaries and between beneficiaries of federal and state health programs.

The panelists agreed that there is concern that longstanding disparities in cancer care will widen further if patients with NSCLC are not offered the appropriate genetic testing necessary for a complete cancer diagnosis and reiterated that coverage for broad-based biomarker testing in NSCLC could improve treatment delays, appropriate use of targeted therapies, and address health disparities.

**UP NEXT**

This Market Insights program is a critical part of AMCP’s efforts to identify deeper insights to guide coverage, access, and clinical management decisions.

Our next steps will be to:

- Host a webinar with panelist Q&A to share these findings and answer your questions
- Provide educational opportunities around biomarker driven treatment selection in NSCLC
- Develop best practice recommendations through expert interviews, national survey, and workshop
- Communicate best practices through a Partner Session at AMCP Annual Meeting
**Table 5. Summary Framework for Improving Precision Oncology in NSCLC**

<table>
<thead>
<tr>
<th>Biomarker Testing Ordering</th>
<th>Testing Performance</th>
<th>Result Reporting</th>
<th>Treatment Decision</th>
<th>Quality Measurement</th>
<th>Cost Effectiveness</th>
<th>Health Disparities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase awareness of testing guidance with education</td>
<td>Develop standard report formats that can be imported into EMRs</td>
<td>Interpret test results before treatment initiation</td>
<td>Develop process measures from EMR or claims data</td>
<td>Use of evidence-based coverage and value-based reimbursement for broad-based biomarker testing</td>
<td>Support efforts to educate clinicians on health disparities in NSCLC</td>
<td></td>
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<tr>
<td>Develop disease-specific algorithms to select appropriate biomarker tests</td>
<td>Support the use of testing with the quickest reporting times</td>
<td>Check during PA review process that appropriate biomarker testing was completed</td>
<td>Use available published data as a benchmark</td>
<td>Pilot quality-improvement efforts that focus on health equity in oncology care</td>
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</tr>
<tr>
<td>Greater use of laboratory and oncology consultations</td>
<td>Consider reflex use of broad-based biomarker testing</td>
<td>Reference NCCN guidelines for patients needing urgent treatment while biomarker results are pending</td>
<td>Conduct a pharmacy quality check before dispensing/administering medication</td>
<td>Consider national society guidelines to guide coverage for biomarker testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider reflex use of broad-based biomarker testing</td>
<td>Consider use of both tumor and liquid biopsies to improve the timeliness and comprehensiveness of biomarker results</td>
<td>Support the use of shared decision-making</td>
<td>Develop process measures from EMR or claims data</td>
<td>Include the cost of side effects, quality-adjusted life years, health care resource utilization, secondary lines of therapy in cost effectiveness analyses</td>
<td></td>
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</tr>
</tbody>
</table>

“It’s not just about the targeted therapies, it’s really about making better treatment decisions overall. It is important for payers to recognize the value of testing that is in line with clinical treatment guidelines to improve patient outcomes and potentially reduce the total cost of care.”

– Oncologist

**Summary**

The success of precision oncology in improving health outcomes in NSCLC relies on the accurate identification of biomarker-driven therapeutic options and use to guide therapeutic decisions. Payers have a key role in supporting the timely and appropriate access to comprehensive testing and enabling clinicians to determine the optimal treatments throughout the patient journey. Actions encouraged by panelists were identified and organized into a framework for improving precision oncology in NSCLC (Table 5). Key steps to improve appropriate biomarker testing in NSCLC include increasing awareness of biomarker testing guidance with education and the use of reflex broad-based biomarker testing when more than one biomarker-linked therapy is approved for the patient’s disease. Biomarker test results should be interpreted before treatment initiation and guidelines referenced when patients need urgent treatment while biomarker results are pending. Finally, the panelist suggested managed care organizations pilot quality-improvement initiatives that focus on improving adherence treatment guidelines in NSCLC and health equity.
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References


