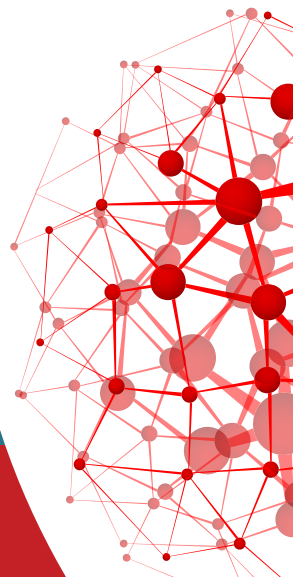


Ongoing Advances & Improvements in **MOLECULAR TESTING**



This tool is a benefit of membership.

Association of Community Cancer Centers

MOLECULAR TESTING

Resources & Tools for the Multidisciplinary Team



Funding and support provided by
Pfizer Oncology.



Ongoing Advances & Improvements in Molecular Testing

Recent advances in the application of molecularly-targeted therapies in cancer continue to revolutionize the approach to patient care. Oncologists around the country are applying principles of “biomarker-driven medicine” and tailoring therapies based on specific tumor characteristics to optimize outcomes in patients with cancer. At the same time, molecular testing processes are becoming increasingly complex, especially in community cancer programs where resources and staff are more limited when compared to major academic research centers.

To ensure that cancer programs in the community have guidance around the molecular testing processes for patients with non-small cell lung cancer (NSCLC), the Association of Community Cancer Centers (ACCC), in collaboration with Pfizer Oncology, launched a multi-phased initiative in 2012 titled, *Molecular Testing in the Community Oncology Setting*. The initiative included:

- ACCC member surveys
- Articles in the January/February 2015 *Oncology Issues*
- Onsite learning lab workshops at member programs that identified eight key areas for improvement and developed potential action items for each (see box on page 11)
- An online resource center at www.accc-cancer.org/moleculartesting.

In 2015 ACCC, in collaboration with Pfizer Oncology, launched *Molecular Testing Practice Profiles: Peer-to-Peer Learning*. This project began in March 2015 with a stakeholders meeting where an interdisciplinary panel of clinicians and administrators discussed ongoing advances and improvements in molecular testing (see box at right).

ATTENDEES at the March 2015 *Molecular Testing Practice Profiles: Peer-to-Peer Learning Stakeholders Meeting*

Peter Graze, MD
Medical Oncologist
Annapolis Oncology Center
Annapolis, Md.

Pablo Gutman, MD
*Department Chair,
Pathology*
Holy Cross Germantown Hospital
Medical Director
Cancer Institute Holy Cross Health
Silver Spring, Md.

Danna Johnson, MD
Director of Pathology
Thomas Johns Cancer Hospital,
Johnston Willis Campus
Richmond, Va.

Randall A. Oyer, MD
Oncology, Medical Director
Lancaster General Hospital
Lancaster, Pa.

Gail W. Probst, RN, MS, AOCN
Director of Cancer Services
Huntington Hospital, Don Monti
Cancer Center
Huntington, N.Y.

John W. Summerville, MD
Pathologist
Southside Regional Medical Center
Petersburg, Va.

**Lawrence Wagman, MD, FACS, FPCS
(Hon)**
Executive Medical Director
St. Joseph Hospital of Orange,
The Center for Cancer Prevention
and Treatment
Orange, Calif.



Evolving NSCLC Molecular Testing Guidelines

The National Comprehensive Cancer Network (NCCN) updates its NSCLC clinical practice guidelines several times each year to provide medical oncologists with the most current information to guide treatment decisions. In contrast, the latest guidelines specific to molecular testing in lung cancer (Molecular Testing Guideline for the Selection of Lung Cancer Patients for *EGFR* and *ALK* Tyrosine Kinase Inhibitors) were published in 2013 by the College of American Pathologists (CAP), the International Association for the Study of Lung Cancer (IASLC), and the Association of Molecular Pathology (AMP).¹ In 2014 these guidelines were endorsed by the American Society for Clinical Oncology (ASCO) and medical oncologists around the country accepted these standards to form their molecular testing policies within their institutions.²



Recent advances in the application of molecularly-targeted therapies in cancer continue to revolutionize the approach to patient care.

During the ACCC stakeholders meeting, participants discussed how their cancer programs have been developing their own molecular testing policies and procedures based on the evidence-based recommendations outlined in the CAP/IASLC/AMP guidelines. Pathologists and medical oncologists have formed collaborative working groups to improve lung biopsy processes to ensure that they have sufficient samples to perform the necessary molecular tests outlined in the guidelines. Given recent advances in molecular testing developments and targeted therapies, CAP, IASLC, and AMP recently announced plans to update and publish revised NSCLC molecular testing guidelines in mid-to-late 2016.³ The revisions will include updated information about:

- *ALK* testing recommendations
- *EGFR* and *ALK* resistance
- Emerging molecular targets
- Re-biopsy and repeat analysis in post-treatment relapse.



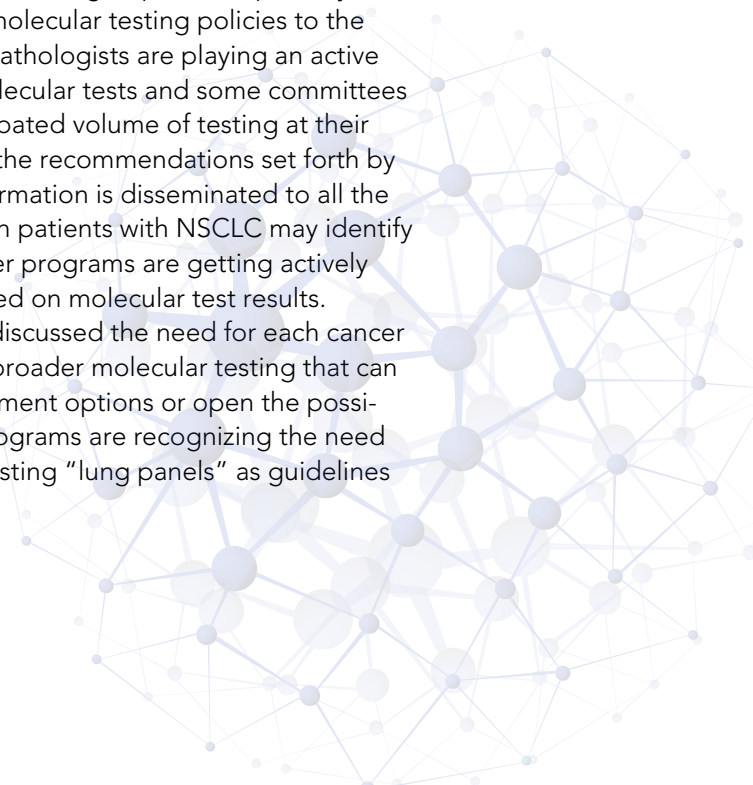
Broader Molecular Profiling for NSCLC

The 2015 NCCN clinical practice guidelines for non-small cell lung cancer mention how strongly the guidelines endorse “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.”⁴ The complex issue of broader molecular profiling for patients with NSCLC remains an active discussion topic at many community cancer programs. In some cases, broader profiling may not provide clinically useful information that will alter the course of treatment. During the ACCC stakeholders meeting, participants discussed how cancer committees around the country are struggling with the issue of optimizing and balancing the need for actionable test results vs. obtaining data that may not result in any changes in clinical treatment.

Since the lack of physician consensus around molecular testing processes can reduce workflow efficiency and create significant delays, some cancer programs have instituted an interdisciplinary molecular diagnostic subcommittee to focus on the latest developments around specific molecular tests for different tumor types. These groups meet quarterly and provide leadership, direction, and guidance on molecular testing policies to the cancer committee and to executive leadership. Pathologists are playing an active role in evaluating the clinical utility of various molecular tests and some committees are performing cost analyses based on the anticipated volume of testing at their program. Once the cancer committee approves the recommendations set forth by the molecular diagnostic subcommittee, the information is disseminated to all the medical staff. Since broader molecular profiling in patients with NSCLC may identify rare driver mutations, pathologists in some cancer programs are getting actively involved in clinical trial selection for patients based on molecular test results. Participants at the ACCC stakeholders meeting discussed the need for each cancer program to examine how to effectively perform broader molecular testing that can also be tailored to identify potential clinical treatment options or open the possibility for research opportunities. Some cancer programs are recognizing the need to be flexible so they can customize molecular testing “lung panels” as guidelines evolve and new therapies emerge.



The complex issue of broader molecular profiling for patients with NSCLC remains an active discussion topic.





Partnerships with Academic Research Centers

Cancer programs actively engaged in clinical research are expanding their partnerships with major academic research centers and referring patients with rare driver mutations for clinical trials. These growing partnerships often include collaboration and communication with researchers via teleconference and interactive video conferencing. These hybrid meetings combining live and interactive digital communication allow clinicians in the community to stay current and educate their team members about advances in cancer treatments. Furthermore, these interactions facilitate stronger research partnerships which will become increasingly important as widespread lung cancer screening programs identify more patients with early-stage disease. Some of these patients may have rare driver mutations that are being studied in clinical trials.



Hybrid meetings combining live and interactive digital communication allow clinicians in the community to stay current...

One example of a structured community-academic partnership is the “molecular tumor board.” In this model, academic centers provide a way for community-based oncologists to interact with academic expert clinicians, basic scientists, geneticists, and bioinformatics and pathway scientists. Since most oncologists have not been formally trained in advanced genomics, they may have difficulty understanding how to interpret certain molecular test results. In the setting of a molecular tumor board discussion, a panel of experts may comment about the complex molecular profiles that pertain to each patient. The discussion may explain how the genomic sequencing information could optimize clinical treatment decisions or identify patients for clinical trials.

One published study evaluating the clinical efficacy of a molecular tumor board noted how their complex cancer patients had a median of four molecular abnormalities, but no two patients had the same genetic aberrations.⁵ The researchers noted that this type of information could truly help to personalize cancer treatment plans if the team of clinicians better understood the significance of each patient’s genomic sequencing results. As more community-based cancer programs form partnerships with research centers to gain access to expert clinicians and scientists, the collaborative discussions pertaining to complex molecular test results and unique patient characteristics may alter the course of treatment plans and improve outcomes in patients with NSCLC.

10 ACTIONABLE TAKEAWAYS for Cancer Programs

- 1. Consider developing your own molecular testing policies and procedures** based on evidence-based recommendations, such as those discussed on page 2.
- 2. Since the lack of physician consensus around molecular testing processes can reduce workflow efficiency** and create significant delays, consider instituting a multidisciplinary molecular diagnostic subcommittee to focus on the latest developments around specific molecular tests for different tumor types.
- 3. Examine how to effectively perform broader molecular testing** that can also be tailored to identify potential clinical treatment options or open the possibility for research opportunities.
- 4. Implement a process to measure your performance** and improve the quality of your molecular testing practices and clinical treatment patterns.
- 5. Consider adding molecular testing results** directly into your tumor registry as structured, expandable data fields so that you can periodically perform audits and reviews of test utilization and results.
- 6. Invest resources and time to educate your staff and patients** about the importance of molecular testing in patients with NSCLC.
- 7. Educate the physicians performing lung biopsies** about the importance of obtaining adequate tissue for molecular testing; forward-thinking cancer programs are already anticipating the growing need to potentially biopsy very small suspicious lung masses detected during lung cancer screening.
- 8. Form a collaborative working group**—composed of pathologists and medical oncologists—to improve lung biopsy processes to ensure that you have sufficient samples to perform the necessary molecular tests outlined in your guidelines.
- 9. If your program is actively engaged in clinical research**, consider developing or expanding a partnership with a major academic research center, including collaboration and communication with researchers via teleconference and interactive video conferencing. This type of partnership will let your clinicians stay current and educate your team members about advances in cancer treatments.
- 10. Consider hosting an outreach event**—for example, a one-day conference to teach the public about lung cancer prevention, screening, and treatment—to increase the overall visibility of your cancer program in the community and strengthen relationships with primary care providers and referring clinicians.



Staff & Patient Education

Cancer programs are investing more resources to educate their staff and patients about the importance of molecular testing in patients with NSCLC. Some programs offer regularly scheduled “lunch and learn” education sessions where they discuss the clinical importance of how molecular test results may impact care plans. By dedicating this time each week or month, cancer programs are making the investment to educate nurses, medical assistants, and other office staff about how best to communicate with patients when using complex terms like “biomarker-driven medicine” or “biomarker-driven therapies.”

Patients are also requesting additional information about how advances in lung cancer treatments may be applicable to themselves or their loved ones. This demand for knowledge and education by patients became accelerated when President Obama announced the Precision Medicine initiative (see page 10) and described how this type of approach is revolutionizing cancer care in America. Some cancer programs are devoting an outreach day to educate the patients in their communities and they are organizing and hosting one-day

conferences to teach the public about lung cancer prevention, screening, and treatment. These outreach events can increase the overall visibility of the cancer program in the community and strengthen relationships with primary care providers and referring clinicians. These events also open up opportunities to identify patients who may be at high risk for lung cancer by raising public awareness about the clinical benefits of lung cancer screening and early detection.



Outreach events can also increase the overall visibility of the cancer program in the community and strengthen relationships with primary care providers and referring clinicians.



Obtaining Adequate Biopsy Samples for Molecular Testing

Cancer programs are still faced with the challenge of obtaining adequate biopsy samples for molecular testing. Greater efforts are being made to educate physicians performing lung biopsies about the importance of obtaining more tissue for molecular testing. As a result, more radiologists are performing CT-guided lung biopsies using core biopsy needles instead of relying solely on fine-needle aspiration (FNA). Also, many community-based pulmonologists are making greater efforts to use advanced bronchoscopy techniques, including endobronchial ultrasound (EBUS). Some hospitals are even investing in navigational bronchoscopy equipment and training for their pulmonologists and surgeons.

Some cancer programs have recognized the need for a more formal, structured way to ensure that lung biopsies are adequate for molecular testing. Forward-thinking cancer programs are already anticipating the growing need to potentially biopsy very small suspicious lung masses detected during lung cancer screening. As a result, some have developed a protocol specifically for small-tissue acquisition. This algorithmic tool serves to guide multidisciplinary groups of physicians who are trying to decide how best to obtain biopsy samples when the tumor is very small.

PEER-TO-PEER LEARNING WEBINARS

These webinars are part of *Molecular Testing Practice Profiles: Peer-to-Peer Learning*, a collaborative initiative between ACCC and Pfizer Oncology. Access these archived webinars at www.accc-cancer.org/moleculartesting.

The Tissue Issue—Sampling & Testing

Hear strategies for developing and implementing biomarker testing policies and procedures. Learn about the potential need for repeat biopsies when disease returns to look for new mutations or resistance patterns in the recurring tumor.

The Deal with Data—Collecting & Sharing

Strategies to standardize reporting and develop EHR work arounds. Hear how to use technology to share information between key stakeholders. Tips for improving clinical workflow and communication. Learn how to perform costs analyses and evaluate the value of molecular tests and cancer treatment options.

The Future of Molecular Testing—Decreasing Costs & Increasing Expectations

Strategies to implement biomarker-driven medicine and cancer genetics into your program. Learn about collaborative opportunities with academic research centers, including how to leverage their resources and expertise in your community. Tips for keeping up with rapidly evolving clinical practice guidelines.



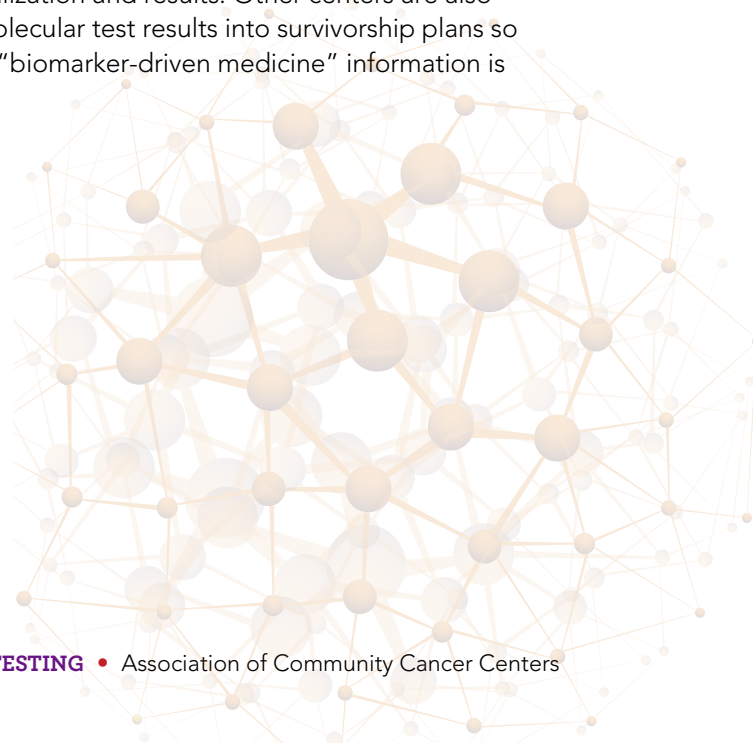
Discussing Value in Oncology

In the context of potentially expensive diagnostic studies and therapies, the discussion of value in oncology becomes challenging to clearly define. In 2012 the ABIM (American Board of Internal Medicine) Foundation, along with *Consumer Reports*, launched the Choosing Wisely campaign to address rising concerns pertaining to medical treatment overuse, unnecessary testing, and medical waste.⁶ In 2013 and 2015, the ABIM Foundation received grants from the Robert Wood Johnson Foundation to advance Choosing Wisely and help physicians and patients engage in conversations about reducing unnecessary medical tests and procedures.

Over the past several years, ASCO has been working on the ASCO Value Initiative under the leadership of the ASCO Value in Cancer Care Task Force, which was established in 2007. Their team is developing a framework for evaluating the relative value of new cancer treatment regimens across three domains: treatment efficacy, toxicity, and cost. ASCO has identified three goals for its value initiative:⁷

1. Oncologists will have the skills and tools needed to assess relative value of interventions and use these in discussing treatment options with their patients.
2. Patients will have ready access to information that assists them in selecting high-value treatments that meets their unique needs.
3. Those responsible for covering the costs of cancer care will have a useful algorithm with which to define and assess the value of cancer treatment options.

Cancer programs in the community are devoting more resources to measure their own performance and improve the quality of their molecular testing process and clinical treatment patterns. They are measuring how often a repeat lung biopsy is being obtained because of inadequate tissue for molecular testing from the first biopsy. Some cancer programs are adding molecular testing results directly into their tumor registry as structured, expandable data fields so that they can periodically perform audits and reviews of test utilization and results. Other centers are also incorporating patient records and molecular test results into survivorship plans so that they can communicate how this “biomarker-driven medicine” information is directing their care plans.





The Future Direction

As cancer programs in the community embrace the era of biomarker-driven medicines, they are recognizing the growing importance of clearly establishing policies and procedures to optimize molecular testing that will direct appropriate clinical treatment decisions. Pathologists are standardizing molecular test results and improving the efficiency of their reporting formats for medical oncologists. However, the lack of interoperability across different electronic health record (EHR) systems remains a significant challenge. Some pathology departments are also evaluating whether they should be performing more complex genomic tests in-house vs. sending the tests out to commercial labs. As the capabilities of diagnostic assays and testing machines improve, the cost of bringing some of those tests in-house may become more feasible and beneficial.

Cancer programs are also recognizing how the future of cancer care will rely more heavily on technology tools and data-driven infrastructures. They are improving the utility of disease registries and data warehouses by designing and implementing quality improvement initiatives around important metrics. Clinical analytics tools that integrate directly with EHR data are providing clinicians with advanced clinical decision support and revealing potential treatment options based on unique patient characteristics and genomic profiling information.

These days, cancer programs administrators and clinicians are spending more time conducting cost analyses and evaluating the value of different cancer treatment options so they can be responsible stewards of important resources. Participants at the ACCC stakeholders meeting noted that the immediate future of oncology care includes the exploration of evolving reimbursement models like the Centers for Medicare & Medicaid Services (CMS) Oncology Care Model and the growing use of technology-driven tools, such as data analytics advanced clinical decision support. As the landscape of cancer treatment incorporates more technology advances in both diagnostic and treatment options, there will be a growing need for leadership and guidance around policies and procedures aimed to balance treatment efficacy, toxicity, and cost.



Cancer programs are recognizing how the future of cancer care will rely more heavily on technology tools and data-driven infrastructures.



Accelerating Towards Precision Medicine

In early 2015 President Barack Obama announced the federal Precision Medicine Initiative in his State of the Union Address. With a proposed budget of \$215 million in the first year, the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Office of the National Coordinator for Health Information Technology (ONC) will drive innovations in genomic sequencing and targeted drug development that will improve the treatment of certain conditions such as cancer. Specifically:⁸

- **\$130 million to NIH** for development of a voluntary national research cohort of a million or more volunteers to propel our understanding of health and disease and set the foundation for a new way of doing research through engaged participants and open, responsible data sharing.
- **\$70 million to the National Cancer Institute (NCI)**, part of NIH, to scale up efforts to identify genomic drivers in cancer and apply that knowledge in the development of more effective approaches to cancer treatment.
- **\$10 million to FDA** to acquire additional expertise and advance the development of high quality, curated databases to support the regulatory structure needed to advance innovation in precision medicine and protect public health.
- **\$5 million to ONC** to support the development of interoperability standards and requirements that address privacy and enable secure exchange of data across systems.

Over the past few years, the landscape of NSCLC treatment has been rapidly evolving to include drug therapies that target specific driver mutations. One of the major goals pertaining to the Precision Medicine Initiative is the creation of a national, patient-powered research cohort of one million or more Americans who will volunteer to participate in research. Given that an estimated 221,200 new cases of lung cancer will be discovered in 2015,⁹ there is a tremendous opportunity to advance precision medicine research in this area so that new treatments may be identified to target different mutations.

KEY AREAS for Improvement & Potential Action Items

IDENTIFIED AREAS FOR IMPROVEMENT

POTENTIAL ACTION ITEMS

Biopsy samples insufficient for molecular testing

- Reach out to programs with effective endobronchial ultrasound (EBUS) procedures and request to let team observe
- Improve fine-needle aspiration (FNA) biopsy results by scheduling meeting with radiologist, pulmonologist, and pathologist to review literature on FNA and discuss the optimal approach
- Review how radiologists are performing CT-guided lung biopsies and identify opportunities to standardize, make improvements in techniques, and increase appropriate use of core needle over FNA
- Compare adequacy rates of core needle biopsy samples vs. FNA Molecular tests not ordered for eligible patients

Molecular tests not ordered for eligible patients

- Review individual charts to determine why patients were not tested
- Discuss findings with team and consider ways to make improvements for future patients
- Review how disease staging impacts reflexive molecular testing process
- Create a reflexive molecular testing process

Lack of pathology-driven reflexive molecular testing

- Develop and implement a reflexive molecular testing pathway
- Update process and policy to include:
 - Simultaneous testing for *EGFR* & *ALK*
 - Documentation of why *EGFR* & *ALK* were not completed
 - Create process and tools for monitoring

Clinicians not capturing and documenting key quality measures for reporting

- Add molecular testing results to cancer registry as structured data fields
- Improve documentation around specific National Quality Forum (NQF), American Society of Clinical Oncology (ASCO), Quality Oncology Practice Initiative (QOPI) or other validated quality measures
- Revise progress notes templates or add tabs, fields, and/or sections so that nurses and physicians are consistently documenting information in EHR
- Include document of completion for molecular testing, along with test results
- Define process or create a template to assure inclusion of documentation of the reason for not completing testing

Lack of standardized reporting formats for molecular test results

- Standardize the application of the College of American Pathologists (CAP) lung biomarker reporting template in the EHR system

Difficulty using the cancer registry to measure molecular testing quality

- Add *EGFR* and *ALK* test results into cancer registry as a structured data field which will allow periodic review of molecular testing rates in an easier, more efficient manner
- Develop more uniform approach for entering NSCLC information into registry

Lack of an established pathway when evaluating a suspicious lung mass

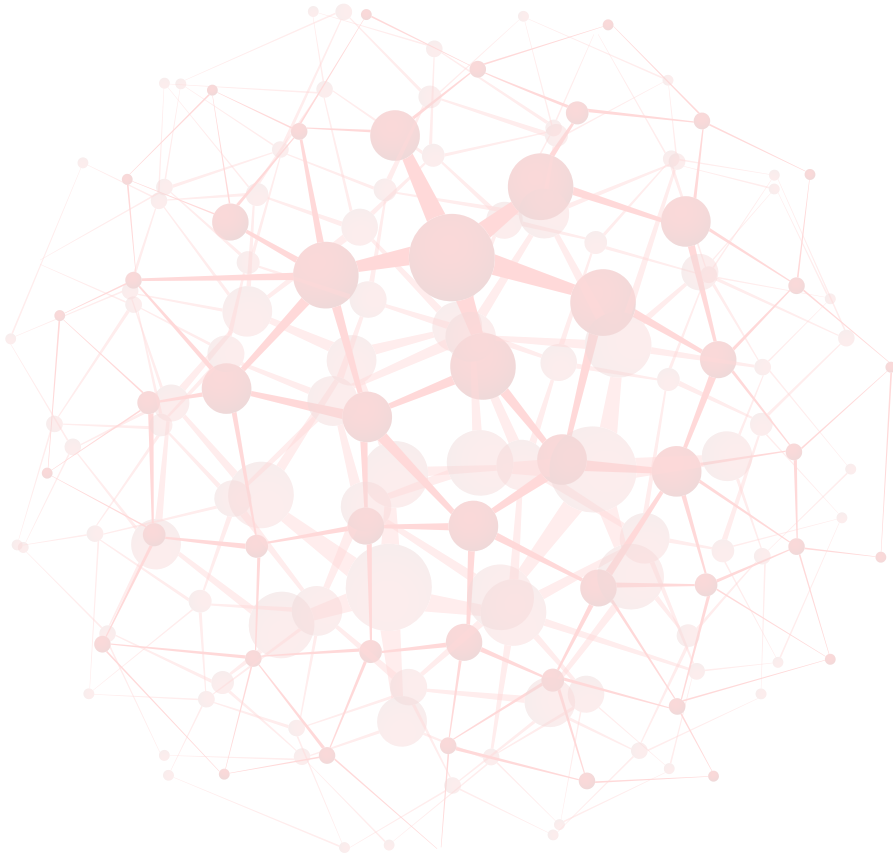
- Monitor lung cancer patient data obtained from imaging reports, pathology reports and surgical reports, to include size of lesion, location of lesion, and mode of biopsy to see if there are patterns that drive mode of biopsy decisions
- Include information about a lung "hotline" to report abnormal chest x-ray and CT scan reports for radiology charts
- Include lung "hotline" information on patient instruction forms for chest X-ray or CT scan

Delays when ordering molecular tests for inpatients due to the CMS "14 Day" rule

- Working with senior administration to develop an approved center policy for molecular testing for inpatient diagnosis; educating staff and physicians about policy

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About the Association of Community Cancer Centers

The Association of Community Cancer Centers (ACCC) serves as the leading advocacy and education organization for the multidisciplinary cancer care team. Approximately 20,000 cancer care professionals from 1,900 hospitals and practices nationwide are affiliated with ACCC. Providing a national forum for addressing issues that affect community cancer programs, ACCC is recognized as the premier provider of resources for the entire oncology care team. Our members include medical and radiation oncologists, surgeons, cancer program administrators and medical directors, senior hospital executives, practice managers, pharmacists, oncology nurses, radiation therapists, social workers, and cancer program data managers. For more information, visit ACCC's website at www.accc-cancer.org. Follow us on Facebook, Twitter, LinkedIn, and read our blog, ACCCBuzz.

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Association of Community Cancer Centers

A publication of the Association of Community Cancer Centers
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Funding and support provided by
Pfizer Oncology.