Lung cancer is the most common cause of cancer death in both men and women. In fact, it is estimated that nearly 230,000 lung cancer cases will be diagnosed in the United States in 2020. Of those cases, 80-85% of lung cancer is non-small cell lung cancer (NSCLC).
The treatment of patients with NSCLC has become reliant on tissue and/or blood biomarkers to help guide treatment decisions.

**What are biomarkers?**

Biomarkers are objective and measurable biological components that shed light on underlying processes involved in the development and progression of diseases. For example, we are familiar with common biomarkers: high cholesterol is indicative of developing coronary artery disease and high blood sugar is telling of diabetes. The science of biomarker research of NSCLC accelerated in the early 2000s, culminating with identification of additional genetic biomarkers to aid the care of lung cancer patients. In 2020, lung cancer therapy involves a complex array of biomarker assessments that can help inform physicians’ treatment decision-making.

“Think of a biomarker as a fingerprint specific to a molecular or genomic alteration, or mutation,” says Stan Krulewicz, senior medical director in the oncology division of Pfizer’s U.S. Medical Affairs. “The cancer tumor cell, whether it’s lung cancer or any other type of cancer, creates a unique fingerprint with the biomarker, through its metabolism at the molecular level.”

Identifying as many biomarkers as possible has been a collective goal for oncologists, scientists, and researchers for decades. Biomarkers provide investigators a more complete story about a patient’s cancer: its genetic characteristics, how aggressive it is, and how it interacts with the immune system. In the past, cancer treatment was typically the same regardless of what type or stage of lung cancer a patient had. Now, with the help of cutting-edge research and the study of biomarkers, patients have a greater chance of receiving advanced treatment options that are personalized to treat their unique cancer.

“It's important to have proper identification of genomic biomarkers in oncology,” adds Krulewicz. “It's a great opportunity for prescribers and, more importantly, for patients to have a better understanding of the clinical characteristics of a tumor and also provide biomarker-directed therapies in the lung cancer setting.”

**How to test for biomarkers in NSCLC**

Biomarker testing, also known as mutation, genomic, or molecular testing, is done in two ways: tissue biopsy and liquid biopsy. Tissue biopsy—the more traditional and most used
method—involves obtaining a tissue sample directly from the tumor.

A liquid biopsy involves analyzing a blood sample to look for cancerous cells; it plays a significant role in biomarker testing and offers several advantages over testing tissue samples. Results from a liquid biopsy may help to complement results obtained from tissue; therefore, experts like Krulewicz recommend using it in conjunction with tissue biopsies, which can lead to more precise treatment options for patients.

“In the past, [scientists] were looking for a single gene in which they’d run a single diagnostic panel,” he explains. “But now, with next-generation sequencing, multiple genes can be run on the same panel at the same time.” Next-generation sequencing makes interpreting data even more complex, “but there's a greater chance that a biomarker oncogene could be identified,” says Krulewicz.

Biomarker test results help a patient’s health care team understand as much as possible about a patient's unique lung cancer and whether there is a U.S. Food and Drug Administration (FDA)-approved biomarker-drug therapy or an appropriate clinical trial that may target their unique lung cancer. Identifying a patient's biomarkers can result in a more targeted and personalized treatment plan.

**Biomarkers specific to NSCLC**

The evolution of biomarkers therapy began in 2004 when the FDA approved a medicine to treat EGFR mutated NSCLC. Since then, scientists have identified more than 20 different driver alterations (which contribute to cancer development) that are specific to lung cancer. Most of those are within a subtype of NSCLC, called lung adenocarcinoma. Of those driver alterations or biomarkers, nine are treatable through FDA-approved therapy drugs: EGFR, ALK, ROS1, BRAF V600E, NTRK, MET, RET, including PD-L1.

Additional research is needed to identify and help treat the approximately one-third of lung cancer patients for which biomarkers have yet to be identified. “Imagine a pie having multiple slices: we currently have about 12 slices associated with lung adenocarcinoma, which comprises approximately 66% of the pie,” explains Krulewicz. “There still remains the opportunity to advance the science by identifying the remaining unknown mutations. We're always striving in the discovery area to fill out the remainder of that pie.”
How biomarkers are used to make lung cancer treatment decisions

Confirming a patient's biomarker status can open the door to precision medicine. “There are now multiple biomarker-defined patient subgroups, with evidence showing that treatment with targeted therapies results in better clinical outcomes when compared with traditional chemotherapy for people living with these cancers,” says Krulewicz. “That is the ultimate goal.”

Biomarkers are used to help determine the best treatment options for a person with lung cancer, whether that’s through targeted drug therapy or a specific immunotherapy drug.5

Ultimately, precise predictive biomarker testing is still being developed and additional research is needed to discover more. “We are continuing to conduct segmentation of patient types that actually harbor these [unknown biomarkers],” says Krulewicz. “One of Pfizer's commitments is to be on the leading edge of this through our internal research, our academic partnerships, as well as our work with patient advocacy organizations. Also, to adapt additional medicines to become FDA- and regulatory authority-approved medicines that could be recommended for treatment.”

For biomarker-driven therapies yet to be FDA-approved, clinical trials may be available and an appropriate option, depending on the patient's individual case. “The whole goal is identifying the right patient with the right mutation and helping them get the right therapy at the right time,” says Krulewicz.

References:


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