Breakthrough Technology Spurs New Test for Non-Small Cell Lung Cancer Patients

Last month in *Expert Edge*, Mary Bronner, MD, discussed how circulating cell-free tumor DNA (ctDNA) is revolutionizing cancer care. This month, ARUP Laboratories Medical Director Wade Samowitz, MD, focuses on the specific application of this technology for non-small cell lung cancer (NSCLC) patients using the newly available clinical test: *EGFR T790M* Mutation Detection in Circulating Cell-Free DNA by Digital Droplet PCR.

About 85 percent of lung cancers are non-small cell lung cancers. Overall, lung cancer is the deadliest cancer for both men and women in the United States and claims more lives than colon, breast, and prostate cancer combined, according to the American Cancer Society.

Dr. Samowitz, who oversees Solid Tumor Molecular Diagnostics and Histology at ARUP Laboratories, is also a professor of pathology at the University of Utah School of Medicine. He specializes in gastrointestinal pathology and the molecular genetics of colorectal cancer, and oversees numerous molecular tests in solid tumor oncology, including single-gene assays and next-generation sequencing.

Q: How is this test (*EGFR T790M*) being applied in helping with the care for NSCLC patients?

A: Resistance commonly develops in NSCLC patients treated with targeted therapy against *EGFR* mutations. The T790M is the most common resistance mutation. If this mutation is detected, then therapy can be changed to a drug that is active against the T790M alteration.

Q: When should a clinician order this test and what kind of information will it provide?

A: A clinician should order this test if resistance to targeted therapy develops in a patient with NSCLC. Serial monitoring for the T790M mutation may detect it before it is clinically evident and allow for a more timely change in therapy.

Q: How will the results of the test change the standard of care for these patients?

A: It will lead to a change in therapy to better target this mutation.

Q: Is this mutation usually seen at the time of primary diagnosis?

A: Although there is some controversy regarding this, the typical scenario is the mutation is not seen at presentation but develops following targeted therapy as a resistance mechanism.

Q: How does this test allow us to monitor tumor developments in lung cancer patients?

A: Lung cancer sheds its mutated DNA into the blood and new, highly sensitive technologies, such as digital droplet PCR, allow for its detection in minimally invasive blood samples. This test can detect lung cancer recurrence as well as tumor resistance to early generation tyrosine kinase inhibitor chemotherapy drugs, and permit personalized chemotherapy for the T790M mutation.

Q: What previous methods were used for solid tumor testing and what advantages does circulating cell-free tumor DNA testing offer?

A: Previous methods included various imaging modalities with or without tissue sampling.

Cell-free tumor DNA testing of a blood sample is less expensive and potentially more sensitive than imaging, and allows us to look for resistance mutations that can guide therapy. Cell-free tumor DNA testing is also less invasive than tissue sampling, and the so-called "liquid biopsy" allows for sampling of the entire tumor burden rather than just one site.

Tumor heterogeneity may lead to a false negative if only one site is sampled; cell-free tumor DNA testing potentially circumvents the problem of tumor heterogeneity and therefore may be more sensitive for the detection of resistance mutations.

Q: How does circulating cell-free tumor DNA testing differ from circulating tumor cell (CTC) testing?

A: Cell-free DNA testing is much more sensitive than circulating tumor cell testing.