Most Young Lung Cancers Patients Have Targetable Genes

By Bryant Furlow

Seventy-five percent of patients diagnosed with metastatic adenocarcinoma of the lung before age 40 have an actionable mutation, according to preliminary results from the Genomics of Young Lung Cancer Study.

“Thus far in our prospective series, those diagnosed with primary non–small-cell lung cancer (NSCLC) under age 40 tend to have stage IV adenocarcinoma and the most commonly found mutations are ALK rearrangement, EGFR activating mutation, and ROS1,” reported lead study author Barbara J. Gitlitz, MD, of the University of Southern California Keck School of Medicine in Los Angeles.

Patients diagnosed with primary NSCLC “tend to be never-smokers” and to be diagnosed with stage IV adenocarcinoma, she reported. Patients younger than age 40 often face long delays in diagnosis “because lung cancer was never considered in the differential diagnosis of their symptoms,” she noted.

Gitlitz reported preliminary findings based on the first 68 study participants. Median age was 35 (age range: 16–39 years) and 35 participants were female, she said.

Sixty patients had been diagnosed with adenocarcinoma, seven had squamous cell lung cancer, and one patient had small-cell lung cancer. Seventy-nine percent were diagnosed with advanced metastatic disease while 21% were diagnosed with stage I–III lung cancers.

ALK rearrangements were present in 50% of males and 38% of females, Gitlitz noted.

“For the 50 participants with stage IV adenocarcinoma, there was a high prevalence of EGFR and ALK at study entry,” she said.

Gitlitz’s team suspected that patients diagnosed with lung cancer before age 40 might be more likely to have tumors that harbor targetable genomic alterations.

“Primary lung cancer is increasingly seen as a heterogeneous disease made up of genomically defined subtypes requiring distinct treatment strategies,” Gitlitz said. “We hypothesized young age at diagnosis is a clinical characteristic associated with an increased chance for a targetable genomic alteration.”

Starting in July 2014, the researchers enrolled patients with bronchogenic lung cancer younger than age 40 at diagnosis to study representation of seven genomic alterations of interest, based on the Lung Cancer Mutational Consortium: EGFR, KRAS, HER2, BRAF, ALK, ROS1, and RET. The team prospectively characterizes the somatic and germline genomics of young lung cancer, and participants who are wild type for all seven genes will undergo additional genomic profiling using the FoundationOne Heme test to help identify “novel oncogenic drivers,” Gitlitz said.

“Our goals are to identify a genomically enriched subtype of lung cancer, facilitate delivery of targeted therapy, and lay groundwork for further studies of heritable and environmental lung cancer risk factors,” Gitlitz said.

Patient eligibility criteria for the study include age < 40 at the time of lung cancer diagnosis, pathologically confirmed bronchogenic lung carcinoma (small cell-lung cancer [SCLC] or NSCLC), regardless of stage, at any point in treatment. For patients with stage IV non-squamous NSCLC, EGFR and ALK genotyping must be performed by a CLIA-certified laboratory before a patient can enroll in the study. A study Web site allows “virtual consenting” for patients who wish to participate remotely.