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Ros1 gene fusions found in 2.4% of Asian patients with lung adenocarcinoma, associated with young age at diagnosis

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ROS1 fusion genes were successfully detected independent of gender or smoking history in young East Asian patients with lung adenocarcinoma, a histological subgroup in non-small cell lung cancer (NSCLC), using multiplex reverse transcriptase-polymerase chain reaction (RT-PCR) and immunohistochemistry (IHC) diagnostic tests.

In NSCLC treatment algorithms, a personalized therapy approach is now being taken based on the genetic characteristics of the cancer. Patients with specific oncogenic molecular aberrations, for example EGFR mutations and ALK gene fusions, respond well to drugs that target these molecular abnormalities. ROS1 is another potential oncogenic molecular driver and this target is sensitive to crizotinib, a drug approved for the treatment of ALK gene fusion NSCLC patients.

Researchers from the National Taiwan University Hospital examined 160 surgical specimens from early-stage lung adenocarcinoma and 332 specimens of fluid around the lungs (malignant pleural effusions) from late-stage lung adenocarcinoma patients. They initially examined these specimens for EGFR and KRAS mutations as well as ALK gene. Specimens that were negative for these three oncogenic drivers were then examined for ROS1 fusions using RT-PCR and IHC. Fluorescence in situ hybridization (FISH) was used if there was a discrepancy between RT-PCR and IHC.

As reported in the August issue of the *Journal of Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer, ROS1 fusions were found in 12 (2.4%) of the 492 specimens examined using the RT-PCR test and 11 of these were also positive for protein expression using IHC. One case had insufficient material remaining for IHC evaluation. Cases negative for ROS1 by RT-PCR as well as negative for EGFR, KRAS, and ALK were evaluated for ROS1 by IHC and, of the 143 cases examined, 116 provided results. Five cases were positive by IHC then using FISH to resolve the discrepancy 1 case was FISH positive, 3 were negative and 1 case had insufficient material. ROS1 positive patients, with a median age of 45 years, were significantly younger (p=0.001) than the entire population, which had a median age of 65, but there were no associations with gender or smoking history. There did not appear to be any survival differences between the ROS1 positive patients compared to the ROS1 negative population.

"The present study demonstrates that RT-PCR and IHC can successfully identity ROS1 gene fusion expression in both surgical and malignant pleural effusion specimens of lung adenocarcinoma without EGFR/ALK/KRAS mutations and the prevalence of ROS1 is similar to that found in other ethnic groups, which may help facilitate a diagnostic algorithm to identify patients who may benefit from a specific targeted-therapy" says Dr. Pan-Chyr Yang, MD, PhD, senior author of the study.

Provided by International Association for the Study of Lung Cancer