Clinical Use

• Assess potential for response to crizotinib therapy in patients with non-small cell lung cancer (NSCLC)

Clinical Background

Lung cancer is the leading cause of cancer-related deaths in the United States, and NSCLC accounts for over 85% of all cases.1 Some NSCLC patients may benefit from targeted drug therapy based on specific genetic alterations in their tumors. One such alteration is rearrangement of the gene encoding anaplastic lymphoma kinase (ALK), a receptor tyrosine kinase that activates signaling pathways involved in cell proliferation and survival. ALK rearrangements have been linked to tumor formation and NSCLC.2 Treatment with crizotinib (XALKORI®), Pfizer, a targeted receptor tyrosine kinase inhibitor, leads to tumor shrinkage or stable disease in most NSCLC patients harboring ALK rearrangements.3

The ROS1 gene, a close evolutionary relative of ALK, encodes a receptor tyrosine kinase that activates some of the same signaling pathways as ALK. ROS1 rearrangements lead to constitutively active fusion proteins and are detected in 1% to 2% of NSCLC cases. They are rarely found concurrently in the same NSCLC tumors as EGFR, KRAS, or ALK mutations. These findings have led to investigations of ROS1 fusion proteins as targets for crizotinib therapy.4-6 Crizotinib has demonstrated in vitro activity against cell lines containing ROS1 rearrangements and has also shown clinical activity based on case studies: patients with NSCLC and ROS1 rearrangements demonstrated shrinkage of tumors in response to crizotinib.4-6 Although crizotinib is currently indicated only for patients with ALK-positive NSCLC,7 clinical guidelines suggest that this drug may also be used for patients with ROS1 rearrangements.1

Similar to ALK rearrangements, most ROS1 rearrangements occur in adenocarcinomas of NSCLC patients, typically in younger never or light smokers.4,8 It is important to note that not all patients with ROS1 rearrangements display these clinical characteristics and not all patients with these characteristics have ROS1 mutations.4 Thus, molecular testing is necessary to identify NSCLC patients who harbor ROS1 rearrangements.

Individuals Suitable for Testing

• Patients with NSCLC who are being considered for crizotinib therapy

Method

• Fluorescence in situ hybridization (FISH) testing with ROS1 break-apart probes to detect rearrangements.9
  - Probes of different colors are hybridized to the 5’ and 3’ regions of ROS1 at the 6q22 locus.
  - Cells are scored for separation of the probes, which indicates ROS1 rearrangement.

Interpretive Information

Detection of ROS1 rearrangements in patients with NSCLC suggests eligibility for treatment with the tyrosine kinase inhibitor crizotinib. During therapy, acquisition of additional, secondary mutations can confer resistance to crizotinib.10

References


*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

This test was developed and its performance characteristics determined by Quest Diagnostics Nichols Institute. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Performance characteristics refer to the analytical performance of the test.