ASCO: Case of acquired resistance to crizotinib ID'd

June 3 2013

A case of acquired resistance to crizotinib has been described in a patient with metastatic lung adenocarcinoma harboring a *CD74-ROS1* rearrangement, according to a brief report published online June 1 in the *New England Journal of Medicine* to coincide with presentation at the annual meeting of the American Society of Clinical Oncology, held from May 31 to June 4 in Chicago.

(HealthDay)—A case of acquired resistance to crizotinib has been described in a patient with metastatic lung adenocarcinoma harboring a *CD74-ROS1* rearrangement, according to a brief report published online June 1 in the *New England Journal of Medicine* to coincide with presentation at the annual meeting of the American Society of Clinical Oncology, held from May 31 to June 4 in Chicago.

Mark M. Awad, M.D., Ph.D., from the Massachusetts General Hospital Cancer Center in Boston, and colleagues describe a case of resistance to crizotinib in a patient with metastatic lung adenocarcinoma harboring a *CD74-ROS1* rearrangement.

The researchers reported that the 48-year-old female patient initially showed a dramatic response to treatment, but subsequently developed resistance. Biopsy of the resistant tumor led to identification of an acquired mutation that resulted in a glycine-to-arginine substitution at codon 2032 of the ROS1 kinase domain. By steric interference with drug binding, this mutation conferred resistance to ROS1 kinase inhibition, although the mutation did not lie at the gatekeeper residue. At autopsy, the same mutation was identified in all metastatic sites examined.

"The autopsy performed in this case revealed the presence of the *CD74-ROS1* gene translocation at all sites of disease," the authors write. "It appears that this mutation occurred early in the development of resistance and suggests that a potent inhibitor of this mutant kinase may have been clinically effective after the failure of crizotinib."

The research was funded by Pfizer, the manufacturer of crizotinib.

More information: Abstract
Full Text
More Information