Alectinib (Alecensa) as First-line Option for ALK-positive Lung Cancer

Anaplastic lymphoma kinase (ALK) gene is present on chromosome 2. ALK gene locus undergoes inversion leading to echinoderm microtubule-associated protein-like 4 (EML4) gene and ALK gene fusion resulting in an oncogenic fusion protein (1). The ALK abnormality occurs in ~3-7% of non-small cell lung carcinoma (NSCLC) (2) and generally associates with adenocarcinoma in those who never smoked or smoked occasionally (1). Crizotinib (Xalkori) was the first ALK inhibitor approved by the FDA in 2013 for the treatment of ALK-positive NSCLC patients. However, resistance is noted within about one year of treatment with crizotinib. Ceritinib (Zykadia) and alectinib (Alecensa) second generation ALK inhibitors were later approved as second-line options for ALK-positive metastatic NSCLCs that had progressed on crizotinib or those who could not tolerate crizotinib. More recently, Peters et al (3) have reported the results from a phase 3 trial comparing crizotinib and alectinib head-to-head in treatment-naïve advanced ALK-positive NSCLC patients. They randomized 303 such patients to receive alectinib (600 mg BID) or crizotinib (250 mg BID). Progression-free survival was the primary endpoint that was determined by investigators. Secondary endpoints included progression-free survival, time to CNS progression, objective response rate and overall survival as determined by independent review committee. Their results revealed that alectinib exhibited better efficacy and lower side effects than crizotinib. Furthermore, alectinib was more effective in preventing brain metastases than crizotinib. Thus, alectinib appears to be better first-line option for the treatment of ALK-positive NSCLC. Accordingly, the FDA has now approved alectinib as a first-line option for ALK-positive metastatic NSCLC.

M. Saeed Sheikh
Department of Pharmacology,
State University of New York,
Upstate Medical University,
Syracuse, New York

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