

Analysis Identifies Cutoff Point for ALK Positivity in Lung Cancer

Jul 23, 2018

Patients with ALK-positive non–small-cell lung cancer (NSCLC) derive benefit from crizotinib across the range of percentages of ALK-positive cells, according to a new study. This supports the clinical utility of using 15% positive cells as a cutoff for ALK positivity, though there is a small number of patients near that cutoff who merit further study.

“In clinical studies of crizotinib, ALK status was determined using fluorescence in situ hybridization (FISH), where $\geq 15\%$ of tumor cells demonstrating a pattern of ALK probe hybridization indicative of gene rearrangement was considered to meet the criteria for defining ALK-positive NSCLC,” wrote study authors led by Jean-Charles Soria, MD, PhD, of the Gustave Roussy Cancer Campus in France. “Assessment of the clinical utility of the 15% FISH cutoff and its relationship to clinical outcomes has been limited by the small number of patients with ALK-positive NSCLC near the 15% ALK-positive cutoff.”

The researchers conducted a pooled analysis of three large clinical trials to better assess the utility of the cutoff; of 11,081 screened patients treated with crizotinib, 1,958 (18%) met the criteria for ALK positivity, 7,512 (68%) were ALK-negative, and 1,540 (14%) had uninformative test results. The results of the analysis of this cohort were [published](#) in *Annals of Oncology*.

The median percentage of ALK-positive cells among the positive population was 58%; among ALK-negative patients, the median percentage of positive cells was 2%.

The objective response rate (ORR) for all ALK-positive patients treated with crizotinib was 55%. This was similar across subgroups, though the small group with 15% to 19% of ALK-positive cells (66 patients) had an ORR of 38%. Among 19 patients with exactly 15% ALK-positive cells, the ORR was 37%. Measured as a continuous variable, higher percentages of ALK-positive cells were significantly associated with better ORR ($P = .002$).

“Patients identified as ALK positive, including those with borderline positive scores (15%–19% ALK-positive cells), demonstrated a clinically meaningful ORR with crizotinib,” the authors wrote. “Overall, these results further support the clinical utility of using ALK FISH testing that employs a cutoff of 15% ALK positivity in identifying patients with ALK-positive NSCLC who benefit from treatment with crizotinib.” They added that though these results were specific to crizotinib, there is no biological reason they would not also apply to treatment with any other ALK inhibitor

CANCER NETWORK