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TARGETED THERAPIES

J-ALEX hints at new first-line in NSCLC

A better understanding of the genetic landscape of non-small-cell lung cancer (NSCLC) has improved the management of this disease. Crizotinib is the standard first-line therapy for patients with *ALK* rearrangements. Upon disease progression, second-generation ALK inhibitors are available, such as alectinib that targets certain resistance mutations, which develop in response to crizotinib. Although alectinib is more selective for ALK and can penetrate the blood–brain barrier, the promising activity of this agent had not been assessed in a randomized head-to-head trial.

Now, result of the J-ALEX study, published in the *Lancet,* have demonstrated a significantly prolonged progression-free survival (PFS) for Japanese patients with *ALK*-positive NSCLC treated with alectinib compared with crizotinib. In this trial, 207 patients who were chemotherapy-naïve or who had received one line of chemotherapy, but not an ALK inhibitor, received either 300 mg alectinib or 250 mg crizotinib twice daily. The median PFS has not yet been reached with alectinib, but was 10.2 months with crizotinib. Moreover, grade 3 or 4 adverse events and dose interuptions were more frequent with crizotinib.

Tomohide Tamura, senior author of the study explains: "this is the first study in *ALK*-positive advanced-stage NSCLC to show the second-generation ALK inhibitor alectinib provides a PFS advantage and is more tolerable than crizotinib". Although these impressive results are encouraging, twice as many patients in the crizotinib arm had brain metastases at baseline. To determine whether this imbalance influenced the efficacy analysis, the authors used stratified Cox-regression analyses, but concluded that it did not influence the results. Whether these data are generalizable to non-Japanese patient populations is unclear. Tamura suggests that "further clinical evaluation in the locally advanced and post-surgical adjuvant treatment settings with alectinib would be desired."

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ORIGINAL ARTICLE Hida, T. *et al.* Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): an open-label, randomised phase 3 trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(17)30565-2 (2017)