Alectinib surpasses crizotinib for untreated *ALK*-positive NSCLC

Alectinib was more effective and less toxic than crizotinib in patients with treatment-naive non-small-cell lung cancer (NSCLC) harbouring rearranged *ALK*, according to results from the ALEX trial.

In this international, phase 3 study, Solange Peters (Lausanne University Hospital, Lausanne, Switzerland) and colleagues compared the second-generation ALK inhibitor alectinib with crizotinib in 303 patients with advanced *ALK*-positive NSCLC who were randomly assigned (1:1) to receive either alectinib (600 mg orally twice a day; n=152) or crizotinib (250 mg orally twice a day; n=151).

Progression-free survival was significantly longer with alectinib than with crizotinib (median not yet reached [95% CI 17·7 months to not estimable] *vs* 11·1 months [9·1–13·1]; hazard ratio 0·47 [95% CI 0·34-0·65]; p<0·001). Overall survival could not yet be estimated. Fewer patients reported grade 3 or worse toxicities with alectinib than with crizotinib (63 [41%] *vs* 76 [50%]).

Co-author D Ross Camidge (University of Colorado, Denver, CO, USA) summarised the results of the ALEX study: "Alectinib now displaces crizotinib as the preferred first-line therapy for *ALK*-positive NSCLC." Crediting the influence of the Response Assessment in Neuro-Oncology (RANO) international working group, Camidge noted that the ALEX study was helping to set new standards for lung cancer trial conduct in that it deliberately allowed patients to enroll who had untreated, asymptomatic brain metastases, to more actively capture efficacy in the CNS. Furthermore, all participants received baseline and follow-up body and CNS screening on the same schedule—which meant that patients without CNS disease at baseline could be studied to assess the drugs' abilities to protect against the development of brain metastases. "Alectinib was better than crizotinib both for treating metastases in the brain and for protecting the brain from later developing this site of spread", said Camidge.

Daniel B Costa (Harvard Medical School, Boston, MA, USA) said, "The ALEX study cements alectinib as the new evidence-based oral inhibitor to be used in newly diagnosed cases of advanced *ALK*-positive tumors. Worldwide patterns of drug approvals and cost-effectiveness analyses or considerations will determine when each individual country will have access to alectinib as the initial drug to combat advanced *ALK*-positive lung cancer."

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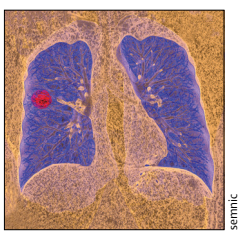

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For the study by **Peters and colleagues** see *N Engl J Med* 2017; published online June 6. DOI:10.1056/NEJMoa1704795

For the **RANO guidelines** see **Review** *Lancet Oncol* 2015; **16:** e270–78