BRIGATINIB IMPROVES PFS OVER CRIZOTINIB FOR ADVANCED ALK-POSITIVE NSCLC

Patients with locally advanced or metastatic ALK-positive non-small-cell lung cancer undergoing their first ALK inhibitor therapy have better progression-free survival with brigatinib than crizotinib

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medwireNews: Brigatinib has achieved significantly longer progression-free survival (PFS) than crizotinib in the ALTA-1L trial of patients with anaplastic lymphoma kinase (***ALK***)-positive non-small-cell lung cancer (**NSCLC**) not previously treated with an ALK inhibitor.

The first interim analysis was performed after a median follow-up of 11.0 months among the 137 patients with locally advanced or metastatic disease who were randomly assigned to receive brigatinib 90 mg/day for 7 days followed by 180 mg/day thereafter, and after a median 9.3 months for the 138 participants who instead were treated with crizotinib 250 mg twice daily.

At this time, the estimated 12-month PFS rate was significantly higher for the brigatinib arm, at 67% versus

43% for the crizotinib-treated patients, and a hazard ratio (**HR**) for disease progression or death of 0.49.

And this was true for patients when classified by age, sex, race, history of tobacco use, ECOG performance status, receipt of prior chemotherapy and the presence of brain metastases at time of study entry, the authors report in *The New England Journal of Medicine*.

For patients with brain metastases at baseline, the median PFS without intracranial progression was unreached for the brigatinib-treated patients versus 5.6 months with crizotinib. The corresponding 1-year rates for this endpoint were 67% versus 21%, giving a HR for intracranial disease progression or death of 0.27 in favour of brigatinib.

Patients given brigatinib were also more likely than their crizotinib-treated counterparts to achieve an intracranial response on a measurable lesion (78 vs 29%) or on any intracranial lesion (83 vs 33%).

At data cutoff, the 1-year rate of overall survival (**OS**) in the brigatinib and crizotinib groups was a comparable 85% and 86%, respectively, and the median value was unreached in both arms.

The ALTA-1L investigators admit that the trial analysis of OS is limited by the opportunity for both crossover from crizotinib to brigatinib in the study and later use of tyrosine **kinase inhibitors** by the participants.

Nevertheless, “[w]ith further follow-up, data in both groups will mature and help to better contextualize the role of brigatinib as compared with other next-generation ALK inhibitors”, say D Ross Camidge, from the University of Colorado Cancer Center in Aurora, USA, and co-authors.

They add that the safety profiles of the two ALK inhibitors were “consistent” with earlier studies, and that there were no cases of clinical pancreatitis.

Grade 3 and more severe adverse events occurred in 61% of brigatinib-treated patients and 55% of those given crizotinib. Interstitial lung disease or pneumonitis of this severity was reported in 3% and 0.7% of patients, respectively, with early-onset events within 14 days of beginning treatment recorded in 3% and 0%, respectively.

Dose reductions were required by 29% of brigatinib arm and 21% of the crizotinib arm, with treatment discontinued because of adverse events in 12% and 9%, respectively.

The study was also presented at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer, held in Toronto, Ontario, Canada.

Reference

Camidge DR, Kim HR, Ahn M-J, *et al*. **Brigatinib versus crizotinib in *ALK*-positive non-small-cell lung cancer** . *N Engl J Med*; Advance online publication 25 September 2018.
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