WCLC 2018: ALTA-1L Trial: Brigatinib vs Crizotinib in Advanced *ALK*-Positive NSCLC

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Key Points

- Brigatinib was associated with improved progression-free survival vs crizotinib.
- Brigatinib was associated with improved intracranial response rates.

As reported at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer (Abstract PL02.03) and in the *The New England Journal of Medicine* by Camidge et al, an interim analysis of the phase III ALTA-1L trial has shown improved progression-free survival withthe next-generation ALK inhibitor brigatinib (Alunbrig) vs crizotinib (Xalkori) in advanced *ALK*-positive non–small cell lung cancer (NSCLC) not previously treated with an ALK inhibitor. Brigatinib was also associated with improved intracranial response rates.

Study Details

In the open-label trial, 275 patients from 124 sites in 20 countries were randomized between April 2016 and August 2017 to receive brigatinib 180 mg once daily after a 7-day lead-in at 90 mg (n = 137) or crizotinib at 250 mg twice daily (n = 138). Randomization was stratified by presence of brain metastases and completion of at least one full cycle of previous chemotherapy for locally advanced or metastatic disease.

The primary endpoint was progression-free survival as assessed by blinded independent central review; the first interim analysis was planned when approximately 50% of 198 expected events had occurred. For the interim analysis, the primary endpoint was tested at a two-sided alpha level of 0.0031.

For the brigatinib vs crizotinib groups: median age was 58 vs 60 years; 50% vs 59% were female; 43% vs 36% were Asian; 61% vs 54% were never-smokers; 94% vs 91% had stage IV disease; 92% vs 99% had adenocarcinoma; 96% vs 96% had Eastern Cooperative group performance status of 0 or 1; 29% vs 30% had brain metastases at baseline; and 26% vs 27% had received chemotherapy for locally advanced or metastatic disease.

Progression-Free Survival

At first interim analysis (after 99 events), median follow up was 11.0 months in the brigatinib group and 9.3 months in the crizotinib group. Estimated progression-free survival at 12 months was 67% in the brigatinib group vs 43% in the crizotinib group (hazard ratio = 0.49, $P < .001$). Median progression-free survival was not reached vs 9.8 months. Hazard ratios (HRs) consistently favored brigatinib across subgroups. On

investigator assessment, progression-free survival at 12 months was 69% vs 40% (HR = 0.45, 95% confidence interval [CI] = 0.30–0.68).

The confirmed objective response rate was 71% vs 60% (odds ratio [OR] = 1.59, 95% confidence interval [CI] = 0.96–2.62). The confirmed intracranial response rate among 39 patients with measureable lesions was 78% vs 29% (OR = 10.42, 95% CI = 1.90–57.05); the intracranial response rate among all 90 patients with brain lesions was 67% vs 17% (OR = 13.00, 95% CI = 4.38–38.61).

Adverse Events

Adverse events of any grade that occurred with a > 5% higher incidence in the brigatinib group included increased creatine kinase (39% vs 15%), cough (25% vs 16%), hypertension (23% vs 7%), and increased lipase (19% vs 12%); those > 5% more common in the crizotinib group included nausea (56% vs 26%), diarrhea (55% vs 49%), constipation (42% vs 15%), peripheral edema (39% vs 4%), vomiting (39% vs 18%), increased alanine aminotransferase (32% vs 19%), decreased appetite (20% vs 7%), photopsia (20% vs 1%), dysgeusia (19% vs 4%), and visual impairment (16% vs 0%). Grade ≥ 3 adverse events occurred in 61% vs 55% of patients, with the most common in the brigatinib group including increased creatine kinase (16%), increased lipase (13%), and hypertension (10%); and the most common in the crizotinib group including increased alanine aminotransferase (9%) and increased lipase (5%). Interstitial lung disease or pneumonitis occurred in 4% vs 2% of patients. Adverse events led to treatment discontinuation in 12% vs 9% of patients. Adverse events led to death within 30 days after the last dose of study drug in 5% of patients in each group.

The investigators concluded: “Among patients with *ALK*-positive NSCLC who had not previously received an ALK inhibitor, progression-free survival was significantly longer among patients who received brigatinib than among those who received crizotinib.”

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