Lung Cancer in Focus

LUNG CANCER NEWS

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Progression-Free Survival Longer With Lorlatinib Than With Crizotinib

Progression-free survival (PFS) is longer with lorlatinib (Lorbrena, Pfizer) than with crizotinib (Xalkori, Pfizer) in advanced ALK-positive non–small cell lung cancer (NSCLC), according to interim results of the CROWN study, by Dr Alice Shaw and colleagues. Lorlatinib is a third-generation ALK inhibitor that was designed to penetrate the central nervous system, whereas crizotinib is a first-generation ALK inhibitor.

The phase 3 study, which appeared in the November 19, 2020, issue of the *New England Journal of Medicine*, enrolled 296 patients with advanced ALK-positive NSCLC who had not received prior systemic treatment for metastatic disease. Patients were randomly assigned to receive lorlatinib (n=149) or crizotinib (n=147) until disease progression, death, or unacceptable toxicity.

The 12-month PFS rate was 78% in the lorlatinib group and 39% in the crizotinib group, with a hazard ratio (HR) for disease progression or death of 0.28 (*P*=.001). The objective response rate (ORR) was 76% in the lorlatinib group and 58% in the crizotinib group. Among the patients with measurable brain metastases, an intracranial response occurred in 82% of those in the lorlatinib group and 23% of those in the crizotinib group. More than two-thirds of the patients in the lorlatinib group (71%) had a complete intracranial response.

The most common adverse events with lorlatinib were hyperlipidemia, edema, increased weight, peripheral neuropathy, and cognitive effects. Grade 3/4 adverse events were more common with lorlatinib (72%) than with crizotinib (56%) "because of the frequent occurrence of altered lipid levels."

Revised Lung Cancer Screening Guidelines Will Partially Address Disparities

Lung cancer incidence and mortality are disproportionately greater in women and minorities, but the 2013 guidelines from the US Preventive Services Task Force (USPSTF) regarding eligibility for lung cancer screening resulted in lung cancer screening rates in these populations that were too low. Now, a cross-sectional study finds that revised screening criteria from the USPSTF will improve—but not erase—existing disparities in eligibility for screening.

In a cross-sectional study that appeared in the January 12, 2021, issue of *JAMA Network Open*, Dr Thomas Reese and colleagues applied the 2013 USPSTF criteria and then the revised criteria (under review in 2020) to respondents to the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System. In the revised criteria, screening for lung cancer is recommended for people 50 to 80 years of age (rather than 55-80 years) who have a smoking history of more than 30 pack-years (rather than 20 pack-years) and are current smokers or who have quit within the past 15 years.

A total of 40,869 people 50 to 80 years old who had a history of smoking were included in the study. The new criteria increased the eligibility rate from 29.4% to 38.3% in men (a 30.3% increase), from 25.9% to 36.4% in women (a 40.5% increase), from 31.1% to 40.9% in Whites (a 31.9% increase), from 16.3% to 28.8% in Blacks (a 76.7% increase), and from 10.5% to 18.7% in Hispanics (a 78.1% increase).

Despite these improvements, "Compared with men, women had lower odds of eligibility, and compared with White [individuals], Black and Hispanic individuals had lower odds of eligibility."

Addition of Chemotherapy to Immunotherapy Improves PFS in PD-L1–Positive NSCLC

The addition of chemotherapy to immunotherapy does not improve PFS, overall survival (OS), or ORR in NSCLC, according to a new meta-analysis, but it does improve PFS among patients whose tumor expression of programmed death ligand 1 (PD-L1) is at least 50%.

The meta-analysis, which was published in *BMJ Open* on November 20, 2020, by Dr Lingling Li and colleagues, included 10 randomized controlled trials of 5765 patients who had received first-line immunotherapy (IO) or immunotherapy plus chemotherapy (IC) for advanced NSCLC. Although no significant differences were found between PFS, OS, or ORR in the 2 groups, the researchers found that PFS was significantly better with IC than with IO in the patients who had tumor PD-L1 expression of at least 50% (HR, 1.81; 95% CI, 1.18-2.78). Furthermore, both PFS and OS were better with IC than with IO in the patients whose tumor PD-L1 expression was at least 1%.

Adverse events were more common with IC than IO, but immune-related adverse events were more common with IO.