FDA Approves Lorlatinib for Second- or Third-Line Treatment of *ALK*-Positive Metastatic NSCLC

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On November 2, 2018, the U.S. Food and Drug Administration granted accelerated approval to lorlatinib (Lorbrena) for patients with anaplastic lymphoma kinase (*ALK*)–positive metastatic non–small cell lung cancer (NSCLC) whose disease has progressed on crizotinib (Xalkori) and at least one other ALK inhibitor for metastatic disease, or whose disease has progressed on alectinib (Alecensa) or ceritinib (Zykadia) as the first ALK inhibitor therapy for metastatic disease. Approval was based on a subgroup of 215 patients with *ALK*-positive metastatic NSCLC, previously treated with one or more ALK inhibitors, enrolled in a nonrandomized, dose-ranging and activity-estimating multicohort, multicenter study (Study B7461001). The major efficacy measures were overall response rate (ORR) and intracranial ORR, according to Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST 1.1), as assessed by an independent central review committee. The ORR was 48% (95% confidence interval [CI] = 42%–55%), with 4% complete responses and 44% partial responses. The estimated median response duration was 12.5 months (95% CI = 8.4–23.7). The

intracranial ORR in 89 patients with measurable central nervous system lesions according to RECIST 1.1 was 60% (95% CI = 49%–70%) with 21% complete responses and 38% partial responses. The estimated median response duration was 19.5 months (95% CI = 12.4–not reached).

The most common adverse reactions (incidence ≥ 20%) in patients receiving lorlatinib were edema, peripheral neuropathy, cognitive effects, dyspnea, fatigue, weight gain, arthralgia, mood effects, and diarrhea. The most common laboratory abnormalities were hypercholesterolemia and hypertriglyceridemia.

According to the approved prescribing information, the recommended lorlatinib dose is 100 mg orally once daily.

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