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Primary and acquired *EGFR* T790M-mutant NSCLC patients identified by routine mutation testing show different characteristics but may both respond to osimertinib treatment

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**Abstract**

Primary *EGFR* T790M mutation is occasionally identified by routine mutation testing in tyrosine kinase inhibitor (TKI)-naive patients with non-small cell lung cancer (NSCLC). We herein aimed to compare the characteristics of primary and acquired T790M mutations in NSCLC patients, and their response to osimertinib. Using amplification refractory mutation system (ARMS) detection, primary T790M was identified in 0.5% (46/8723) of TKI-naive patients, whereas acquired T790M was detected in 49.7% (71/143) of TKI-relapsed patients. T790M always coexisted with a sensitizing *EGFR* mutation. Primary T790M more commonly coexisted with L858R, whereas acquired T790M was more likely to coexist with exon 19 deletions. Moreover, next-generation sequencing (NGS) showed that concomitant sensitizing *EGFR* and primary T790M mutant allele frequencies (MAFs) were highly concordant, but acquired T790M MAFs were significantly lower than the sensitizing *EGFR* MAFs. Sixteen acquired T790M-mutant patients received osimertinib. The median progression-free survival (PFS) was 8.1 months. Four primary T790M-mutant patients received osimertinib and the median PFS was 8.0 months. Together, our study demonstrates that primary and acquired T790M-mutant patients show distinct differences in some clinical and molecular characteristics, but may both respond to osimertinib treatment.