Factors Associated with Occurrence of T790M Secondary EGFR Mutation in Patient with Advanced EGFR-mutant Non-small Cell Lung Cancer Treated with EGFR Tyrosine Kinase Inhibitor

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Background: The most common resistance mechanism to 1 st - or 2 nd -generation EGFR tyrosine kinase inhibitor (TKI) in EGFR-mutant non-small cell lung cancer (NSCLC) patients is the T790M mutation which confers a sensitivity to osimertinib. However, there are limited and inconclusive data regarding predictive factors for the acquired T790M mutation.

Objective: The aim of this study was to identify clinical factors associated with secondary T790M mutation in this population.

Methods: We performed a retrospective study in sensitizing EGFR-mutation, exon 19 deletion or exon 21 L858R point mutation, advanced NSCLC patients who had disease progression following treatment with 1st - or 2nd -generation EGFR-TKI. The primary outcome was to identify clinical parameters associated with the secondary T790M mutation.

Results: We recruited 207 EGFR-mutant lung cancer patients who were diagnosed and received 1st - or 2nd - generation EGFR-TKI between November 2011 and March 2020 and had disease progression. We found the T790M mutation in 138 of 207 patients, 66.7%. With univariate analysis, occurrence of T790M mutation was significantly associated with prior response to EGFR-TKI (OR 2.74, p = 0.006) and progression-free survival longer than 6 months (OR 3.71, p = 0.001). However, only the prior response to EGFR-TKI remained the factor significantly associated with T790M mutation under multivariate analysis (OR 2.61, p = 0.009). The median overall survival in T790M positive patients was 41.9 months, which was longer than those of T790M negative patients, 20.1 months (log rank p-value < 0.001).

Conclusions: Prior response to EGFR-TKI was the factor significantly associated with secondary T790M mutation in patients with EGFR-mutant advanced NSCLC upon disease progression following treatment with 1st - or 2nd - generation EGFR-TKI.