Abstract

Epidural growth factor receptor (EGFR) T790M mutation is associated with EGFR protein kinase inhibitors (EGFR-TKIs) resistance in non-small cell lung cancer (NSCLC). However, tissue availability limits the genotyping of EGFR T790M mutation in a clinical setting. The aims of this study are to develop a blood-based, non-invasive approach to detecting the EGFR T790M mutation in advanced NSCLC patients. Additionally, the plasma concentrations of HGF and sMET, which are also factors associated with EGFR-TKIs resistance, will be examined.

Methods: Blood samples were collected from NSCLC patients with activating EGFR mutations, who were resistant to EGFR-TKIs treatment. EGFR T790M mutations were detected using a droplet-digital PCR (ddPCR) system and plasma DNA. The plasma concentrations of HGF and soluble MET (sMET) were determined using enzyme-linked immunosorbent assays. The relationships between the EGFR T790M mutation status and the concentrations of HGF and sMET, the progression-free survival (PFS), and the overall survival (OS) were analyzed.

Results: Twenty-one (35%) of the patients had EGFR T790M mutations in their plasma DNA as detected using the ddPCR system. No correlations between the post-T790M status and the post-HGF and sMET levels were seen. The PFS and OS of patients with the EGFR T790M mutation were significantly shorter than those of patients without the EGFR T790M mutation (P = 0.03 and 0.04, respectively).

Conclusions: The ddPCR system is a useful method for determining the plasma EGFR T790M mutation status. The combination of the EGFR T790M mutation status, as detected using ddPCR, and the amphiregulin levels may be useful for monitoring drug resistance and for making a prognosis.