Acquired T790M resistance do afatinib in EGFR mutated lung adenocarcinoma

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LETTER TO THE EDITOR

It is still not apparent whether the acquired resistant mechanism of afatinib is same as those in the first-generation TKIs. We show herein an acquired afatinib resistant patient with appearance of T790M mutation.

The patient was a 73-year-old female who had neversmoked and who had received a diagnosis of stage IV lung adenocarcinoma. In direct sequence method, the resected tumor specimen revealed Ex19 E746_A750del (deletion - IN frame) 2235_2249del15 (Deletion). But T790M mutation was not detected in the specimen. This patient, not previouslytreated with gefitinib or erlotinib, had afatinib at a 40-mg dose. Uponstarting the drug administration, primary tumor and pulmonary metastases lesions responded well to the treatment. Eventually, however, 11 months after the initiation of afatinib therapy she developed a recurrent pleural metastaticnODULES and increased pleural fluid that initially responded to afatinib (progressive free survival: 10 months). The T790M mutation, which were not present in the pretreatment tumor tissue, as well as the same Ex19 mutation as that found before treatment were identified in tumor cells from the pleural aspirate.

Afatinib, a second-generation irreversible EGFR-TKI, is approved for treatment of patients with non-small cell lung cancer (NSCLC) harboring activating EGFR mutations. T790M mutation is considered to be the major mechanism of acquired resistance to first-generation EGFR-TKIs in patients with NSCLC. At present, however, appearance of T790M after afatinib...
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therapy as well as acquired resistance to afatinib have been evaluated only in a very small number of patients (1,2). It is still unknown whether T790M mutation has a strong relationship with the acquired resistant mechanism of afatinib and is the major mechanism of acquired resistance not only to first generation TKIs but also to afatinib. In a treatment strategy including next-generation TKIs such as AZD9291, it is important to clarify the resistant frequency of T790M for afatinib.

REFERENCES
