doi • 10.5578/tt.22081
Tuberk Toraks 2016;64(4):317-318
Geliş Tarihi/Received: 22.02.2016 • Kabul Ediliş Tarihi/Accepted: 06.03.2016

Acquired T790M resistance do afatinib in EGFR mutated lung adenocarcinoma

Kunihiko MIYAZAKI¹
Shinya SATO¹
Takahide KODAMA¹
Hiroaki SATOH²
Nobuyuki HIZAWA³

¹ Division of Respiratory Medicine, Ryugasaki Saiseika Hospital, Mito Medical Center, Ryugasaki, Japan

¹ Ryugasaki Saiseika Hastanesi, Mito Tıp Merkezi, Göğüs Hastalıkları Bölümü, Ryugasaki, Japonya

² Division of Respiratory Medicine, Tsukuba University, Mito Medical Center, Mito, Japan

² Tsukuba Üniversitesi, Mito Tıp Merkezi, Göğüs Hastalıkları Bölümü, Mito, Japonya

³ Division of Respiratory Medicine, Tsukuba University, Mito Medical Center, Mito, Japan

³ Tsukuba Üniversitesi, Mito Tıp Merkezi, Göğüs Hastalıkları Bölümü, Tsukuba, Japonya

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 IVlung 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

Yazışma Adresi (Address for Correspondence)

Dr. Hiroaki SATOH
University of Tsukuba, Division of Respiratory Medicine,
Mito Medical Center, MITO - JAPAN
e-mail: hirosato@md.tsukuba.ac.jp

therapy as well as acquired resistance to afatinib have been evaluated only a very small number of patients (1,2). It is still unknown whether T790M mutation has 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

1. Kim Y, Ko J, Cui Z, Abolhoda A, Ahn JS, Ou SH, et al. The EGFR T790M mutation in acquired resistance to an irreversible second-generation EGFR inhibitor. *Mol Cancer Ther* 2012;11:784-91.
2. Katakami N, Atagi S, Goto K, Hida T, Horai T, Inoue A, et al. LUX-Lung 4: a phase II trial of afatinib in patients with advanced non-small-cell lung cancer who progressed during prior treatment with erlotinib, gefitinib, or both. *J Clin Oncol* 2013;31:3335-41.