A Case of Advanced Pulmonary Adenocarcinoma Harboring HER-2 Amplification Treated with Afatinib

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Abstract

HER-2 amplification is a rare mutation and potential target in the treatment of pulmonary adenocarcinoma (AC). Clinical efficacy of HER-2 targeted agent has been reported for AC with HER-2 exon 20 insertion; however it remains unknown for those with HER-2 amplification. Here we report a case of advanced AC harboring HER-2 amplification treated with afatinib, and objective response and symptom improvement were observed.

Keywords: Afatinib; HER-2 amplification; Interstitial lung disease; Lung cancer; Pulmonary adenocarcinoma

Keypoints

- HER-2 amplification revealed by next generation sequencing could be a new therapeutic target for advanced pulmonary adenocarcinoma.
- Pulmonary adenocarcinoma harboring HER-2 amplification could respond to afatinib.

Introduction

HER-2 (also called Cerb-2, Erbb-2 or neu) is an emerging treatment target for non-small cell lung cancer (NSCLC). NSCLC with HER-2 mutation (mainly exon 20 insertion) responds to HER-2 targeted agent (such as trastuzumab, afatinib). HER-2 gene amplification occurs in 3.2-7.4% of pulmonary adenocarcinoma (AC) [1,2]. However, efficacy of HER-2 targeted agent in this group of patients remains unknown. Here we report a case of AC with HER-2 amplification treated with afatinib (Gilotrif, Boehringer-Ingelheim, Germany) [3].

Case Report

A 61-year-old man complaining chronic cough and dyspnea was diagnosed with high-grade AC that originated from lower lobe of left lung and metastasized to bilateral lungs and mediastina lymph nodes. Amplification Refractory Mutation System (ARMS) using tissue biopsied from left lung mass showed wild-type EGFR, ALK, ROS1, and KRAS. 4 cycles of First-line chemotherapy with pemetrexed plus carboplatin resulted in disease progression and worsened dyspnea. Another gene test with ARMS using ctDNA confirmed wild-type EGFR, ALK, ROS1, BRAF, KRAS, MET and RET. Patient refused second-line chemotherapy, and another ctDNA gene test with next generation sequencing (NGS) found HER-2 amplification (copy number, CN=4.13) (Table 1) in addition to wild type EGFR, ALK, ROS1, BRAF, KRAS, MET and RET. Patient received oral afatinib (40 mg once daily) (Figure 1).

Four days after the start of afatinib, dyspnea was ameliorated remarkably. After 24 days, chest CT showed tumor size reduced by 23%, using response evaluation criteria in solid tumors (RECIST) 1.1 and no side effect was observed. His performance status (PS) was improving from 3 to 1. However, on day 42 patients was hospitalized due to recurrent dyspnea, and afatinib was stopped. Chest CT on day 48 showed severe interstitial lung disease (ILD), without significant tumor progression (Figure 2). Patient died on day 65.
Discussion

HER-2 is a member of the HER family of proteins containing four receptor tyrosine kinases that mediates proliferation and differentiation of normal epithelial cells. The overexpression of HER-2 and its gene amplification occur in a minority of patients with NSCLC [1-3], contribute to tumor growth and predict a worse survival [4,5]. Overexpression of HER-2 determined by immunohistochemistry (IHC) was reported in 9.0% of AC [1]. However, some studies showed that gene amplification detected by FISH was more specific than IHC [10,11]. Hence, the efficacy of HER-2 targeted agent in AC with HER-2 gene amplification remains unknown.

Afatinib, an irreversible epidermal growth factor receptor (EGFR)–HER-2 dual inhibitor, has strong antitumor activity in HER-2-amplified lung cancer cell lines [12], mainly through binding with the HER-2 kinase domain and preventing HER-2 from forming heterodimers [13-15] blocks downstream signaling and prevents tumor proliferation. In a case report, HER-2 gene amplification was suggested as a possible mechanism of resistance to afatinib [16].

This patient is diagnosed with advanced AC harboring Her-2 amplification detected by NGS. Considering the efficacy and risk of second-line chemotherapy in patients with poor PS, we start afatinib with consent from the patient. Objective response was observed along with improved symptoms and PS. Although the patient died 2 months after the start of afatinib because of rare (1.5%) but severe side effect of ILD, tumors remains in stable disease. To our best knowledge, this is the first clinical report of afatinib in AC with HER-2 amplification.

Conclusions

Afatinib is a therapeutic option for advanced AC with HER-2 amplification, with its potential side effect of ILD worth noticing.

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References


