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CASE REPORT

# Epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors combined with chemotherapy in first-line treatment in an advanced non-small cell lung cancer patient with EGFR sensitive mutation

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## Abstract

This article demonstrates a case of a lung adenocarcinoma patient in stage IV harboring an epidermal growth factor receptor (EGFR) 19 exon deletion mutation treated with 500 mg/m$^2$ pemetrexed and 75 mg/m$^2$ cisplatin on day 1, sequenced with 250 mg gefitinib on prescription on days 4–28 for six cycles as first-line, then by gefitinib combined with pemetrexed as maintenance therapy. The patient achieved a partial response. Performance status increased from grade 2 to 1. The progression-free survival period was 17 months. Overall survival is now over three years. Side effects of grade two liver dysfunction and dermal toxicity were tolerable. Combined gefitinib with platinum-based chemotherapy as first-line treatment probably benefits non-small cell cancer patients in stage IV harboring sensitive EGFR gene mutations with a better local control rate, longer survival, and tolerable side effects.

## Introduction

Lung cancer has the highest incidence of all cancer types in China.[1] Non-small cell lung cancer (NSCLC) is the most common, with half of the patients ineligible for surgery when diagnosed.[2] For those in stage IV NSCLC, chemotherapy and target therapy are considered as standard first-line treatment according to the National Comprehensive Cancer Network (NCCN, 2015); however, the five-year survival rate is less than 10%.[3]

In this article we share the treatment process of a patient suffering from adenocarcinoma with multiple metastases, in order to discuss a better choice of first-line treatment in advanced NSCLC.

## Case Report

A 41-year-old non-smoking woman presented at the Shanghai Chest Hospital after experiencing a month of dyspnea and two months of left limb movement disorder and verbal ambiguity. She had no past medical history. Her Eastern Cooperative Oncology Group (ECOG) performance status (PS) was grade 2.

The patient underwent testing, including chest computed tomography (CT), which revealed a mass in the left upper lobe beside the aortic arch with multiple metastasis on pleural nodules and pleural effusion (Fig 1), and skull magnetic resonance imaging (MRI), which revealed multiple metastatic brain lesions on the bilateral parietal lobe, left occipital lobe, and right cerebellar hemisphere (Fig 2).

A thoracic puncture was performed and 900 mL of bloody pleural effusion was extracted, which showed lung adenocarcinoma cells with epidermal growth factor receptor (EGFR) 19 exon deletion mutation, negative for anaplastic lymphoma kinase (ALK) and ROS proto-oncogene 1 (ROS-1) fusion gene (Figs 3, 4).

Chemotherapy with 500 mg/m$^2$ pemetrexed and 75 mg/m$^2$ cisplatin on day 1, sequenced with gefitinib 250 mg on

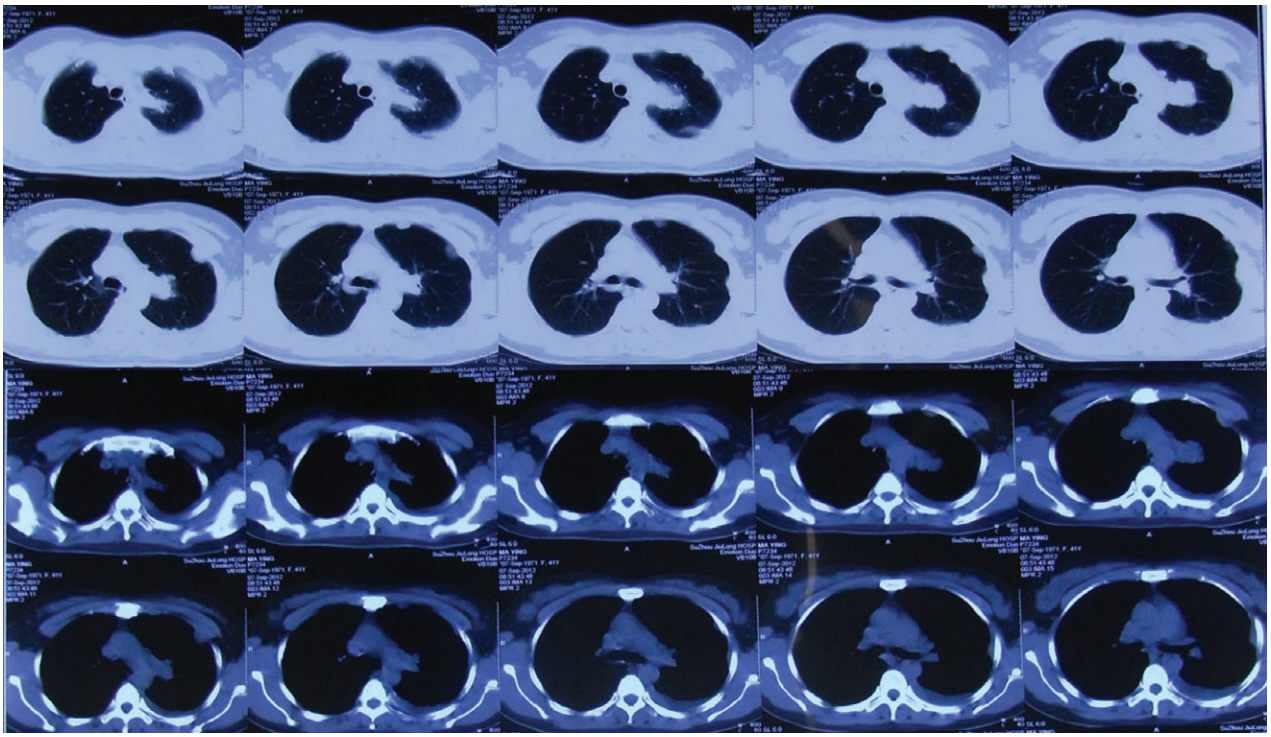

**Figure 1** Chest computed tomography scan before treatment.

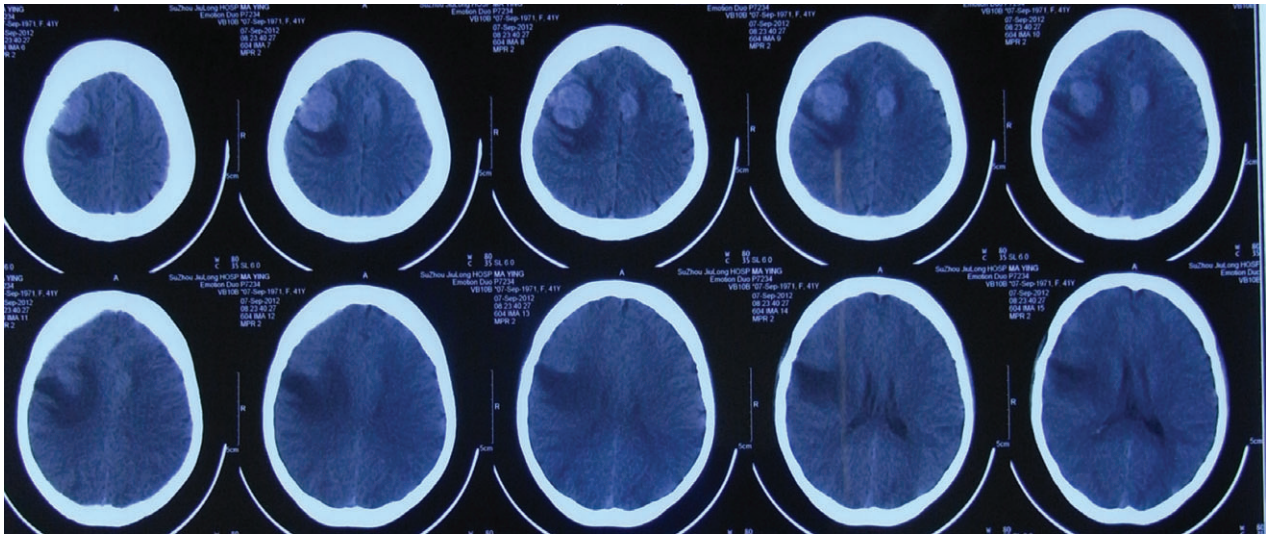

**Figure 2** Brain computed tomography scan before treatment.

prescription days 4–28, was used as first-line therapy. Whole brain radiotherapy (WBRT) 30Gy/10fx was simultaneously applied with the first-line therapy. After six cycles of first-line therapy, the patient achieved a partial response (PR; Fig 5, 6). She felt significant improvement to nervous system symptoms (left limb movement disorder and verbal ambiguity) after two periods of therapy, at which time her ECOG PS was grade 1. During first-line therapy, the side effects included hematologic toxicity (grade 1 neutropenia), liver dysfunction (grade 2, relieved after live protection therapy), and dermal toxicity (grade 2, rashes on face and neck), which we found to be acceptable.

  

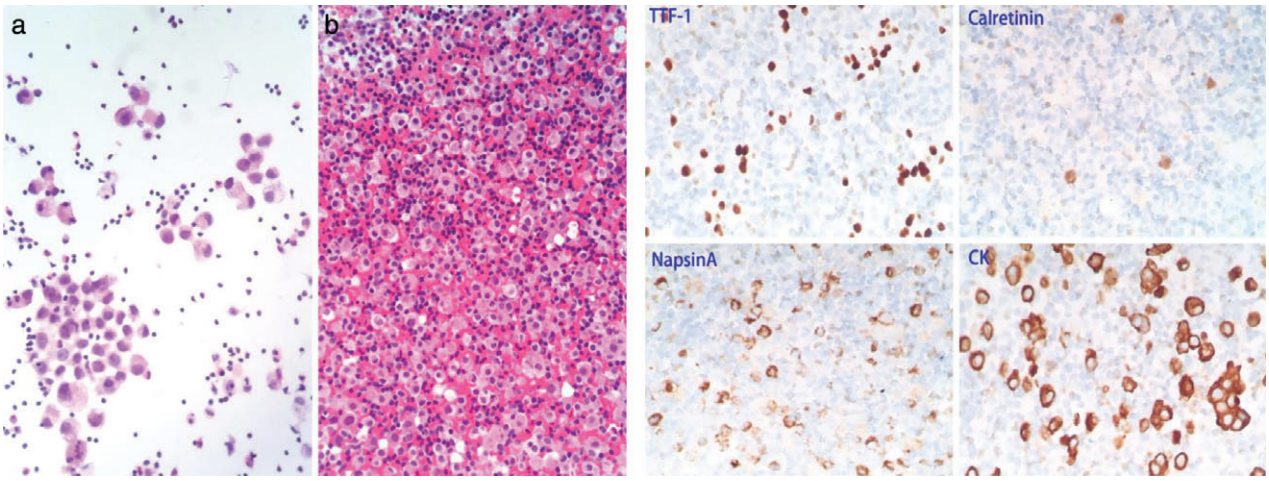


**Figure 3** Histopathology section.

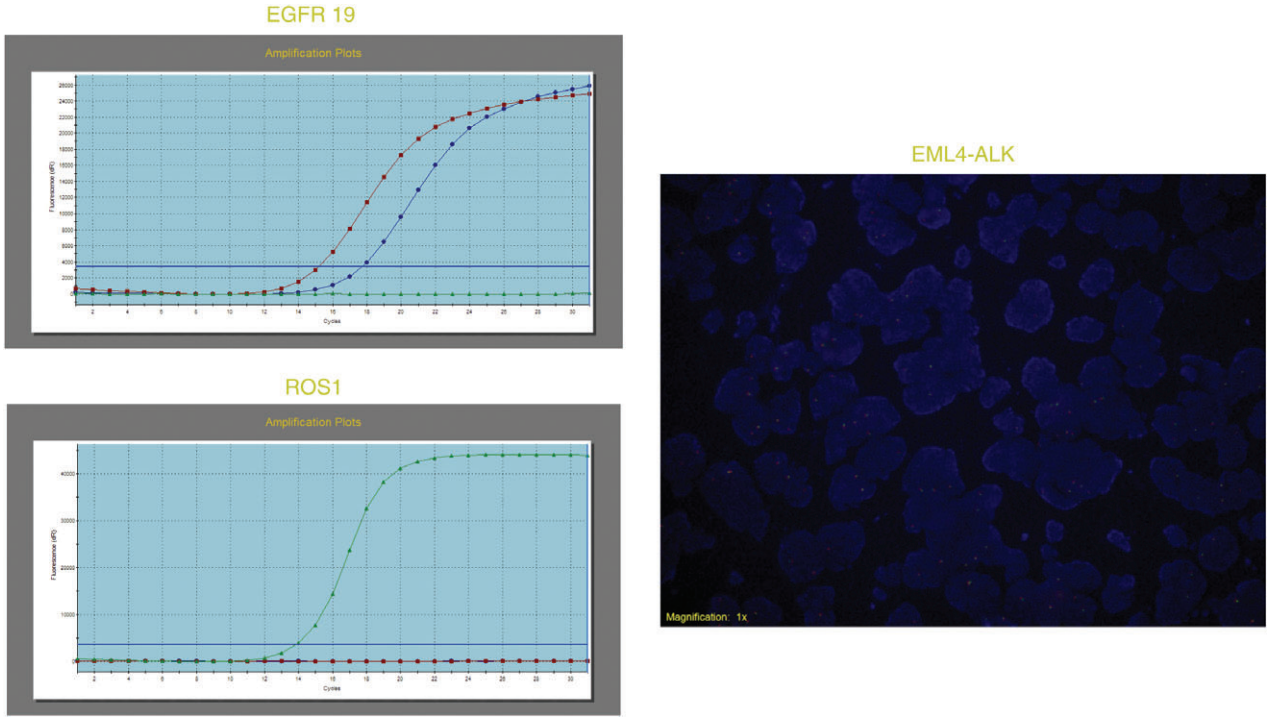


**Figure 4** Genetic testing results.

After six cycles of first-line therapy, the patient received six cycles of maintenance therapy with 500 mg/m$^2$ pemetrexed on day 1, sequenced with 250 mg gefitinib on prescription on days 4–28.

After 17 months of therapy, the patient was found to have progressive disease (PD) with pleural effusion. We proceeded to puncture and drain the pleural effusion and administered second-line therapy: 75 mg/m$^2$ docetaxel combined with 400 mg d[3] bevacizumab. After two months of second-line therapy, the patient still had PD.

The patient has been recruited into a clinical trial of multi-targeted therapy. She remains alive 36 months after the diagnosis of ECOG PS 1.

## Discussion

In this case, a middle-aged woman with no past medical history was found to have multiple metastases on the pleura and in the brain when she was first diagnosed with lung cancer. She suffered from abrupt respiratory and

 

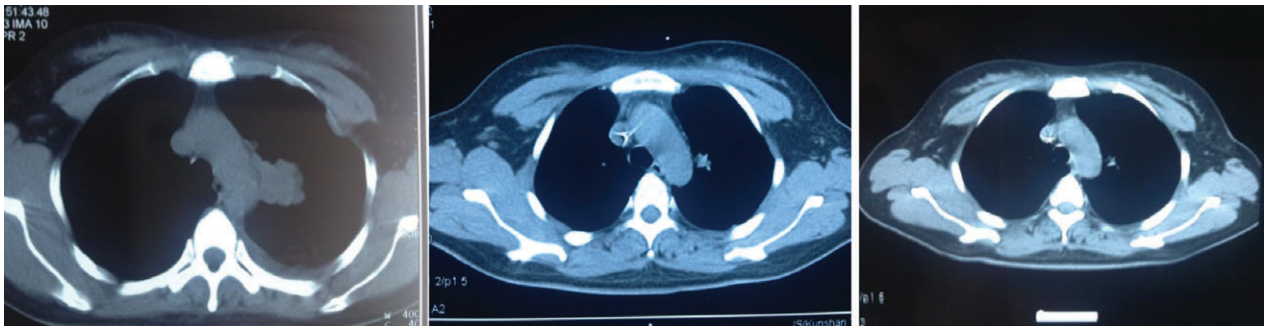

**Figure 5** Chest computed tomography scan during six cycles of first-line therapy.

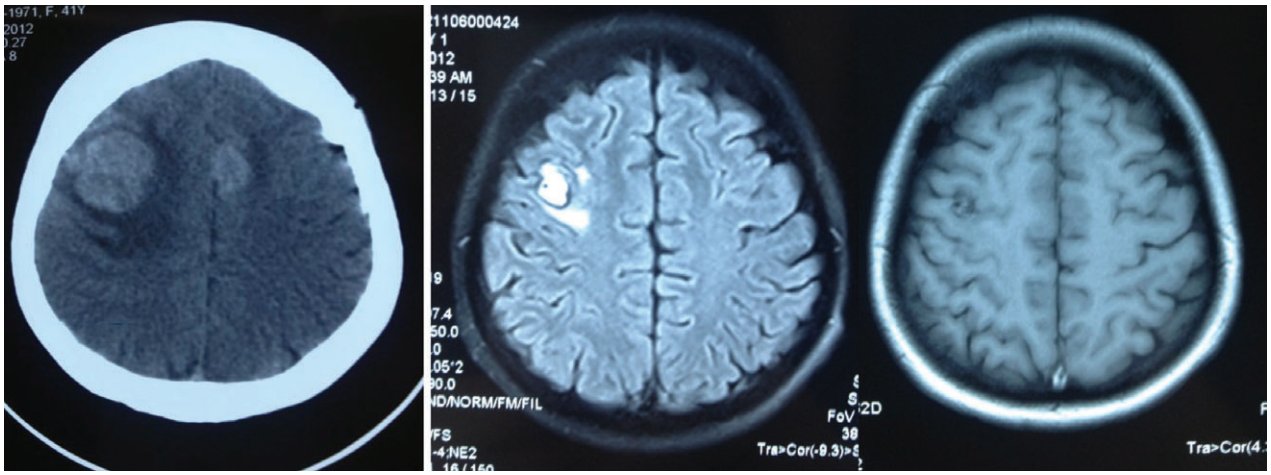

**Figure 6** Brain computed tomography and magnetic resonance imaging scan during six cycles of first-line therapy.

nervous system symptoms, such as dyspnea, left limb movement disorder, and verbal ambiguity. Her PS was grade 2, mainly caused by the tumor in her brain. Our patient's quality of life would be significantly improved if we could relieve the symptoms caused by the tumor. An aggressive decision to treat with combined therapy, an alternative to standard procedure, was made. The response was rapid and effective. The patient's symptoms rapidly improved after first-line chemotherapy combined with target therapy and WBRT. She achieved PR after six cycles of combination therapy. Progression-free survival (PFS) reached 17 months based on maintenance therapy after first-line treatment.

According to the treatment strategy recommended by current guidelines, NSCLC patients without gene mutations benefit from six months PFS after chemotherapy.[3] Patients with EGFR sensitive mutations who receive EGFR-TKI gain a median PFS of 11 months.

The 2004 INTACT 1 study attempted to treat NSCLC with gefitinib combined with chemotherapy, but did not yield positive results as participants were not subject to inclusion criteria.[4] The FASTACT-2 study found that patients with sensitive mutations could benefit from chemotherapy sequenced with EGFR-TKI.[5] A study in our hospital (that has not yet been published) found that in patients with sensitive mutations, PFS after combined therapy reached 20 months, better than the 5.5 months gained by chemotherapy and the 10 months by targeted therapy. Therefore, for EGFR sensitive mutation patients, targeted therapy combined with chemotherapy can extend PFS, reduce drug resistance, and improve therapeutic effect, significantly improving quality of life.

In this case, our patient suffered from reversible liver function damage and grade I bone marrow suppression, which we believe was within acceptable limits. According to meta-analysis, patients who receive combined therapy experience greater toxicity and adverse effects than those who receive single therapy, such as chemotherapy or target therapy, especially older patients and those with underlying diseases. Toxicity and adverse effects include blood toxicity, liver and kidney function damage, and gastrointestinal reaction.[6]

Intensive treatment is not overtreatment. We should assess a patient's general situation and tolerance for

  

degrees of therapy before choosing a therapeutic strategy. More high-level evidence-based medical research is required to confirm our findings.

## Disclosure

No authors report any conflict of interest.

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