

BENEFITS OF ALECTINIB AS FIRST-LINE TREATMENT OF ALK-MUTATED LUNG SQUAMOUS CELL CARCINOMA: A CASE REPORT

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ABSTRACT

Background: Compared with lung adenocarcinoma patients, anaplastic lymphoma kinase(ALK) mutation is relatively rare in patients with squamous cell carcinoma (SqCC). Numerous studies have confirmed that compared with chemotherapy, ALK inhibitors have better efficacy and lower toxicity in the treatment of patients with ALK-mutated advanced lung adenocarcinoma. However, no studies have confirmed the efficacy of ALK inhibitors in patients with ALK-mutated lung SqCC.

Case presentation: We discuss a 76-year-old Chinese man without a history of smoking who came to our hospital for evaluation of severe neck, shoulder blade and right upper limb pain and right lung mass observed on a chest Computed Tomography(CT). According to the results of pathology and immunohistochemistry, the patient was diagnosed as stage IV ALK-mutated lung SqCC. Therefore, the patient used alectinib in the first-line treatment, and achieved obvious effects.

Conclusions: Through this case, we suggest that molecular testing for driver mutations should be considered in lung SqCC patients who are younger, who have a light or no smoking history or mixed histology. Alectinib, as first-line treatment of ALK-positive lung SqCC is a reasonable option.

Keywords: Lung squamous cell carcinoma, anaplastic lymphoma kinase, alectinib.

DOI: 10.19193/0393-6384_2022_1_54

Received March 15, 2021; Accepted October 20, 2021

Background

Research have confirmed the existence of multiple gene mutations in lung cancer, human epidermal growth factor receptor mutations (EGFR) and anaplastic lymphoma kinase (ALK) mutations are the most common. In terms of ALK mutations, it is usually found in about 5% of lung adenocarcinoma patients, although it is extremely rare in lung squamous cell carcinoma (SqCC) ^(1, 2). Studies have confirmed that compared with chemotherapy, ALK inhibitors have better efficacy and lower toxicity in the treatment of patients with ALK-mutated advanced lung adenocarcinoma⁽³⁾.

However, no studies have confirmed the efficacy of ALK inhibitors in patients with ALK-mutated lung SqCC. Therefore, ALK testing is not routinely performed in patients with lung SqCC. Herein, we describe a rare case of ALK-mutated lung SqCC who benefited from alectinib as a first-line treatment.

Case representation

A 76-year-old Chinese man without a history of smoking who came to our hospital for evaluation of severe neck, shoulder blade and right upper limb pain and right lung mass observed on a chest Computed Tomography(CT). The whole body CT results of our

hospital showed tumors in the upper and middle lobe of the right lung with lymphadenopathy in the right hilum, mediastinum, and left supraclavicular fossa (Figure 1a). In addition, head magnetic resonance imaging (MRI) in our hospital suggests brain metastases (Figure 1c). Pathological examination of the CT-guided puncture of the right lung mass biopsy specimen revealed poorly differentiated squamous cell carcinoma. Upon immunohistochemical (IHC) analysis, the tumor cells exhibited strong positive staining for p40 and few positive cytokeratin 5/6, but were negative for thyroid transcription factor-1.

Simultaneously, IHC analysis indicated that the tumor cells were positive for the ALK antibody (Ventana ALK-D5F3-CDx assay) (Figure 2). Based on these findings, the patient was diagnosed with stage IV ALK-positive lung SqCC and was treated with alectinib, a selective ALK inhibitor as a first-line treatment. After 2 weeks of treatment, the symptoms gradually improved.

After 6 months, a follow-up computed tomography scan revealed a remarkable response in the primary lesion (Figure 1b) and significant shrinkage of brain metastases (Figure 1d). At the latest follow-up, 15 months after commencing alectinib treatment, there was no evidence of progression or any remarkable toxicity.

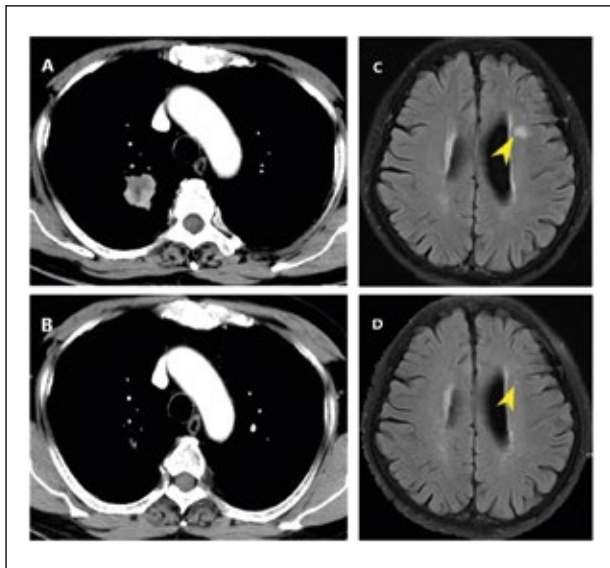


Figure 1: Computed tomography and magnetic resonance imaging findings before and after treatment with alectinib. Before treatment, computed tomography scan revealed (a) a tumor in the upper lobe of the right lung, and magnetic resonance imaging revealed (c) brain metastases (arrow). A computed tomography scan 6 months after commencing treatment revealed (b) a dramatic reduction in tumor size and magnetic resonance imaging revealed (d) almost no brain metastasis (arrow).

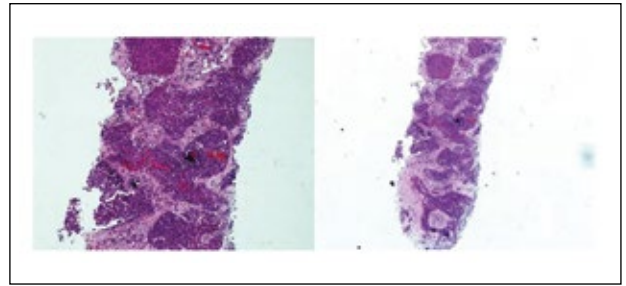


Figure 2: Pathology of lung biopsy specimens guided by Computed tomography.

Discussion and conclusions

In this report, we report a case of ALK-positive lung SqCC with brain metastasis who chose alectinib as the first-line treatment and had significant benefits.

To the best of our knowledge, lung SqCC is one of the common pathological types of non-small cell lung cancer. Gene mutations based on lung SqCC are relatively rare, and therefore the treatment of lung SqCC is still mainly chemotherapy.

However, this does not mean that patients with lung SqCC does not require genetic testing. Studies have shown that molecular testing for EGFR, ALK and ROS-1 alterations should be considered for patients with lung SqCC who are Asian ethnicity, who are younger, who have never smoked, or are former very light smokers or for patients with mixed histology[4]. Compared with chemotherapy, targeted therapy can prolong the progression-free survival and overall survival of patients with lung squamous cell carcinoma⁽⁵⁻⁶⁾. In recent years, with the development of medical treatment, new options have been brought to targeted therapy. Compared with the first-generation ALK inhibitor crizotinib, the second-generation ALK inhibitor alectinib has advantages in efficacy and safety in non-small cell lung cancer, and significantly reduces the event of CNS progression⁽⁷⁻⁸⁾. For patients with non-small cell lung cancer who are found to have brain metastases before treatment, the efficacy of alectinib also has a significant advantage over crizotinib⁽⁹⁻¹⁰⁾. Therefore, ALK-positive non-small cell lung cancer patients with brain metastases can be given priority to choose alectinib for treatment.

In short, molecular testing for driver mutations should be considered in lung SqCC patients who are younger, who have a light or no smoking history or mixed histology. Alectinib, as first-line treatment of ALK-positive lung SqCC is a reasonable option.

References

- 1) Boland JM, Erdogan S, Vasmatzis G, Yang P, Tillmans LS, Johnson MR, et al. Anaplastic lymphoma kinase immunoreactivity correlates with ALK gene rearrangement and transcriptional up-regulation in non-small cell lung carcinomas. *Hum Pathol*, 2009. 40(8): 1152-8.
- 2) Kenmotsu H, Serizawa M, Koh Y, Isaka M, Takahashi T, Taira T, et al. Prospective genetic profiling of squamous cell lung cancer and adenosquamous carcinoma in Japanese patients by multitarget assays. *BMC Cancer*, 2014. 14:786.
- 3) Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med*, 2014. 371(23): 2167-77.
- 4) Hirsch FR, Kerr KM, Bunn PA Jr, Kim ES, Obasaju C, Pérol M, et al. Molecular and Immune Biomarker Testing in Squamous-Cell Lung Cancer: Effect of Current and Future Therapies and Technologies. *Clin Lung Cancer*, 2018. 19(4): 331-339.
- 5) Zhao J, Zhang K, Zhang L, Wang H. [Clinical Efficacy of Crizotinib in Advanced ALK Positive Non-small Cell Lung Cancer]. *Zhongguo Fei Ai Za Zhi*, 2015. 18(10): 616-20.
- 6) Kim YS, Cho EK, Woo HS, Hong J, Ahn HK, Park I, et al. Randomized Phase II Study of Pemetrexed Versus Gefitinib in Previously Treated Patients with Advanced Non-small Cell Lung Cancer. *Cancer Res Treat*, 2016. 48(1): 80-7.
- 7) Hida T, Nokihara H, Kondo M, Kim YH, Azuma K, Seto T, et al. Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): an open-label, randomised phase 3 trial. *Lancet*, 2017. 390(10089): 29-39.
- 8) Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, et al. Alectinib versus Crizotinib in Untreated ALK-Positive Non-Small-Cell Lung Cancer. *N Engl J Med*, 2017. 377(9): 829-838.
- 9) Tomasini P, Egea J, Souquet-Bressand M, Greillier L, Barlesi F. Alectinib in the treatment of ALK-positive metastatic non-small cell lung cancer: clinical trial evidence and experience with a focus on brain metastases. *Ther Adv Respir Dis*, 2019. 13: 1753466619831906.
- 10) Gadgeel S, Peters S, Mok T, Shaw AT, Kim DW, Ou SI, et al. Alectinib versus crizotinib in treatment-naïve anaplastic lymphoma kinase-positive (ALK+) non-small-cell lung cancer: CNS efficacy results from the ALEX study. *Ann Oncol*, 2018. 29(11): 2214-2222.

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