

## Unforeseen Storm: A Case of New Onset Seizures in a Patient on Alectinib For Lung Cancer

Sruthi Sekaran, MD<sup>1\*</sup>, Madiha Ariff, MD<sup>1</sup>, Nithya Ramesh, MD<sup>1</sup>, Vidhi Mehta, MD<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, Trinity Health-Mercy Catholic Medical Center, Darby, PA

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**\*Corresponding author:** Sruthi Sekaran, MD, Department of Internal Medicine, Trinity Health-Mercy Catholic Medical Center, Darby, PA, USA

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### INTRODUCTION

Alectinib is a highly selective, second-generation Anaplastic Lymphoma Kinase-Tyrosine Kinase Inhibitor, FDA-approved in 2017 for ALK-positive non-small-cell lung cancer (NSCLC).

### DESCRIPTION

**Case:** 24-year-old male with history of NSCLC with liver and bone metastases presented with right arm and left leg twitching and weakness for one day. He was started on alectinib two weeks ago, following which he developed a self-limiting allergic reaction manifesting as pruritic rash on his arms. During current presentation, he was hypertensive and tachycardic, with low-grade fever. Labs revealed leukocytosis (11.8/  $\mu$ L), anemia (hemoglobin 9.8 g/dl), and elevated alkaline phosphatase (ALP) of 179 IU/L. CT brain was unremarkable. He tested positive for COVID and was treated with remdesivir. The following afternoon, he developed generalized tonic-clonic seizures (GTCS) and was managed with anti-epileptics. MRI brain showed a small focus of restricted diffusion in right upper precentral gyrus, deemed artifactual versus very small subacute infarction. No brain metastases were noted. Repeat CT brain was negative for infarction. Other imaging showed stable cancer without any progression. EEG demonstrated diffuse mild background slowing without focal or epileptiform activities. Blood, respiratory, and pleural fluid cultures were negative. Patient's seizures were suspected to be due to alectinib.

After multidisciplinary discussion, alectinib was resumed along with levetiracetam on discharge.

### DISCUSSION

Alectinib is the drug of choice for NSCLC with brain metastases due to extensive CNS penetration. Most common adverse reactions (>5%) associated with alectinib include constipation, anemia, fatigue, peripheral edema, dysgeusia and, severe myalgia. Other less common adverse effects are hepatotoxicity, interstitial lung disease, skin allergy, bradycardia, and teratogenicity. There are nearly zero reported CNS side effects.

Alectinib is a highly selective second generation oral inhibitor of anaplastic lymphoma kinase (ALK). It has

shown systemic and central nervous system (CNS) efficacy in the treatment of ALK-EML4 (echinoderm microtubule-associated protein-like 4) fusion protein positive non-small-cell lung cancer (NSCLC). Inhibition of ALK prevents phosphorylation and subsequent downstream activation of STAT3 and AKT resulting in reduced tumor cell viability <sup>[2,3,7]</sup>.

Alectinib showed superior efficacy and lower toxicity in primary treatment of ALK-positive NSCLC with longer period of progression free survival <sup>[4,5]</sup>. The most common proven adverse reactions (>5%) associated with alectinib use are constipation, anemia, fatigue, peripheral edema, dysgeusia and severe myalgia. Other less common adverse effects associated are hepatotoxicity, interstitial lung disease, pneumonitis, skin allergy, bradycardia, elevation of creatine phosphokinase (CPK), and embryo-fetal toxicity <sup>[6-9]</sup>. Alectinib serves as the drug of choice for NSCLC with brain metastasis due to its extensive CNS penetrating capacity. There are nearly zero reported CNS side effects of Alectinib use <sup>[5,7-10]</sup>. This case with a history of recent starting of therapy with Alectinib and development of a focal- converting to generalized tonic clonic seizure with elevated ALP and skin allergy warrants further investigation in this modality of drug adverse effect.

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