# Real World Challenges in managing NSCLC

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## Background

Lung adenocarcinoma with an epidermal growth factor receptor (EGFR) mutation is a well-defined subset of non-small cell lung cancer (NSCLC) that has significantly benefited from targeted therapy with tyrosine kinase inhibitors (TKIs) (Mok et al., 2009). However, factors such as chemotherapy intolerance, financial constraints, and disease progression present challenges in treatment sequencing and long-term disease control (Soria et al., 2018). This case highlights the complexities of managing locally advanced EGFR-mutated lung adenocarcinoma, with multiple treatment modifications due to intolerance, financial limitations, and evolving disease status.

#### **Case Presentation**

A 70-year-old male was diagnosed with locally advanced right lung adenocarcinoma, with an EGFR mutation confirmed via next-generation sequencing (NGS). The patient was initially started on pemetrexed (770 mg) and carboplatin (600 mg), but experienced severe chemotherapy-related toxicities, including profound weakness and periungual hemorrhage, leading to treatment discontinuation. Given the EGFR mutation, gefitinib, a first-generation TKI, was initiated (Maemondo et al., 2010).

However, the patient defaulted treatment in favor of Ayurvedic therapy. On follow-up, PET-CT imaging revealed disease progression, prompting a switch to afatinib, a second-generation TKI (Sequist et al., 2013). Though initially tolerated, the patient developed persistent cough and generalized weakness, with repeat PET-CT confirming further progression. MRI ruled out brain metastases. Given continued disease progression, the patient was advised to switch to osimertinib (80 mg once daily), a third-generation TKI targeting both common EGFR mutations and the T790M resistance mutation (Mok et al., 2017).

However, due to financial constraints, the patient could not afford osimertinib. Instead, the patient was started on second-line chemotherapy (administered on Day 1 and Day 15) as an alternative strategy. After three cycles, the patient demonstrated significant symptomatic improvement. Eventually, the patient secured access to osimertinib, allowing for transition to osimertinib monotherapy, with chemotherapy discontinued. The patient remained clinically stable with no significant adverse effects reported.

### Conclusion

This case underscores the challenges of treatment sequencing, drug affordability, and patient adherence in managing EGFR-mutated lung adenocarcinoma. While chemotherapy intolerance and financial limitations initially impacted treatment decisions, the temporary use of chemotherapy stabilized the patient, enabling an eventual transition to osimertinib, which led to disease control and improved quality of life. This case reinforces the importance of individualized treatment strategies, accessibility to targeted therapies, and financial support mechanisms to ensure optimal patient outcomes. Further research is needed to address the global affordability of third-generation TKIs and determine the best treatment sequencing for EGFR-mutant NSCLC.

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