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Review

Clinical Outcomes and Adverse Effect Management of Sotorasib in a KRAS G12C-Mutated NSCLC Patient

Shivani Modi[1], MD, Supriya Peshin[2*], MD, Shagun Singh[3], MD and Nagaishwarya Moka[4], MD

[1]Jefferson Einstein Healthcare Network, Norristown, Philadelphia, USA

[2]Norton Community Hospital, Virginia, USA

[3]Banner health, Tuscon, Arizona, USA

[4]Lincoln Memorial University, Tennessee, USA

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***Corresponding author:** Dr. Supriya Peshin, Norton Community Hospital, Virginia, USA

ABSTRACT

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, frequently driven by genetic mutations such as KRAS. This case report presents a 67-year-old female patient diagnosed with NSCLC of the right lung, harboring a KRAS G12C mutation. Initial treatment with stereotactic body radiotherapy (SBRT) and chemotherapy was poorly tolerated, leading to the administration of sotorasib, a KRAS G12C inhibitor. The patient experienced adverse effects including severe rash, diarrhea, and acid reflux, necessitating dose adjustments. This report details the clinical course, management strategies for adverse effects, and outcomes in the context of KRAS G12C-mutated NSCLC treated with sotorasib.

Keywords: Sotorasib; Non-small cell lung cancer; Genetic mutation

Introduction

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, often driven by genetic mutations such as KRAS. The KRAS G12C mutation is a specific variant found in a subset of NSCLC patients, for which targeted therapies like sotorasib have been developed. Sotorasib is a KRAS G12C inhibitor that has shown promise in clinical trials. However, its use can be limited by adverse effects requiring dose adjustments and supportive care. This case report details the clinical course, management of adverse effects, and outcomes in a patient with KRAS G12C-mutated NSCLC treated with sotorasib[3,4].

Case Presentation

A 67-year-old female patient was diagnosed with non-small cell lung cancer (NSCLC) of the right lung, classified as CT4, Nx, M1a, with a separate tumor nodule present in the contralateral lobe. Histologically, the tumor was identified as moderately differentiated adenocarcinoma, positive for thyroid transcription factor-1 (TTF-1) and NAPSIN, and negative for P-40, indicating a non-squamous subtype. Molecular profiling revealed a KRAS G12C mutation, which is a specific targetable mutation. Tumor mutational burden (TMB) and microsatellite instability (MSI) status were undetermined, and the programmed death-ligand 1 (PD-L1) expression was low at 1%[5,6].

Initial Presentation

The patient initially presented with lesions in the right upper and lower lobes of the lung. The primary treatment strategy involved stereotactic body radiotherapy (SBRT) to these regions, followed by two cycles of chemotherapy. However, the patient exhibited poor tolerance to chemotherapy, experiencing

significant side effects that necessitated discontinuation of the treatment[7].

Treatment with Sotorasib

Given the KRAS G12C mutation identification, the patient was started on sotorasib, a targeted KRAS G12C inhibitor, at an initial dose of 480 mg daily. However, within a short period, the patient developed a severe rash localized to the intertriginous areas, leading to the discontinuation of sotorasib therapy for five months. After this hiatus, the patient was re-challenged with sotorasib at the same dose of 480 mg daily. Unfortunately, she experienced severe diarrhea, which further complicated her treatment regimen. Consequently, the dose of sotorasib was reduced to 240 mg daily, a better-tolerated level by the patient[8,9].

Management of Adverse Effects

The severe rash experienced by the patient was managed with corticosteroid cream, which led to significant improvement, particularly after the dose reduction of sotorasib. The diarrhea that emerged upon re-challenge at the higher dose also resolved with the decreased dose of 240 mg daily. The patient suffered from severe acid reflux, initially managed with pantoprazole.

However, alternative strategies were employed due to a known interaction between pantoprazole and sotorasib[1,2]. These included advising the patient to take pantoprazole either 4 hours before or 10 hours after taking sotorasib to mitigate the interaction, though this approach was not entirely satisfactory[10,11].

Additionally, the patient reported bilateral shoulder pain, indicative of arthralgias, which was managed with Tylenol. This pain was initially not linked to disease progression, as CT scans did not show any new evidence of disease in the bones[12].

Follow-up and Monitoring

Regular follow-ups with CT and PET scans revealed stable disease in the right lung and small nodules in the left lung, which were too small to be biopsied or showed significant PET uptake. The latest CT scan presented a mixed response: some nodules remained stable while one lesion showed a slight increase in size. The patient's current treatment involves a daily dose of 240 mg of sotorasib, with no new signs of rash and manageable side effects. The patient is scheduled for further PET scans to monitor disease progression and adjustments to her treatment plan will be made based on these findings[13].

Discussion

KRAS mutations, particularly KRAS G12C, are prevalent in NSCLC and pose a challenge due to their resistance to traditional therapies. Sotorasib, a targeted KRAS G12C inhibitor, has shown efficacy in stabilizing disease progression. However, its use can be complicated by adverse effects such as rash, diarrhea, and gastrointestinal issues, necessitating careful management. In this case, the patient's severe rash and diarrhea were managed by reducing the sotorasib dose from 480 mg to 240 mg daily. This dose adjustment significantly improved tolerability while maintaining disease control. The patient's acid reflux, exacerbated by the interaction between sotorasib and pantoprazole, required careful timing of medication administration to optimize both efficacy and symptom management[14,15].

Disease Monitoring

Regular imaging and follow-up were crucial in monitoring the patient's response to treatment. Despite the challenges, the patient achieved disease stabilization with a lower dose of sotorasib, highlighting the importance of personalized treatment strategies in managing adverse effects and optimizing therapeutic outcomes[16].

Conclusion

Sotorasib represents a significant advancement in the treatment of KRAS G12C-mutated NSCLC. This case report illustrates the importance of managing adverse effects through dose adjustments and supportive care to maintain treatment efficacy and improve patient quality of life. Personalized treatment strategies are essential for maximizing the therapeutic potential of sotorasib while minimizing its adverse effects. Further research and clinical experience will help refine these strategies and improve outcomes for patients with KRAS G12C-mutated NSCLC[17,18].

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