Optimizing the Pharmacokinetics of Sonidegib in Small Bowel Syndrome and Advanced Basal Cell Carcinoma: Our Solution

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SYNOPSIS

- Basal cell carcinoma (BCC) is the most common cancer worldwide, with an increasing annual incidence.1-2
- In patients with advanced BCC, lesions become extensively locally invasive or metastatic, and traditional first-line surgical treatment may be contraindicated.3
- Hedgehog pathway inhibitors (HHIs) represent an alternate treatment option for patients with advanced BCC.4
- HHIs block the aberrant Hedgehog pathway activation that allows transcription of glia-associated oncogene transcription factors and activation of target genes for tumorigenesis and angiogenesis during development of BCC (Figure 1).5
- Most HHIs prevent Hedgehog signaling by binding to and preventing activation of transmembrane protein Smoothened.6

METHODS

An N-of-1 trial was conducted

- The patient was an 83-year-old woman with history of short bowel syndrome and dysphagia
- She also had a history of multiple keratinocyte carcinomas of the nose and cheek, which were previously treated with Mohs micrographic surgery, radiation, and salvage radiation
- The patient presented to Strasswimmer Mohs Surgery, Delray Beach, FL, USA with a large, surgically unresectable, recurrent, locally advanced BCC lesion on the nasal tip
- Biopsy of the nose revealed a locally advanced, infiltrative BCC

RESULTS

- After 5 weeks of treatment, reduction in tumor size was noted (Image 1)

B. Improvement of the patient’s infiltrative BCC after 5 weeks of sonidegib treatment

Image 1. Photographs showing tumor response in patient with BCC following sonidegib treatment

A. The patient upon initial presentation with an infiltrative BCC of the nose

OBJECTIVES

- Understand the effects of high-fat foods on sonidegib absorption
- Raise awareness of and improve access to sonidegib for other patients with gastrointestinal absorption issues

CONCLUSIONS

- Around week 5 of treatment, the patient began to experience adverse effects, including mild nausea and muscle cramping of the hands and feet
- Clinical laboratory parameters remained within normal limits
- A 5-week medication holiday was subsequently instituted with symptom resolution
- Tumor regrowth was noted after 5 weeks without therapy, so sonidegib was reinstated at the same dose for another 5 weeks
- In total, the patient completed three 5-week sonidegib cycles with 5 weeks of medication holiday between each cycle
- Following the third course of sonidegib, the patient and her family were satisfied with treatment results
- More than 1 year later, she continues to deny further issues

REFERENCES


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DISCLOSURES

HG, MC, and JS report nothing to disclose.