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Neoadjuvant Sonidegib for the Management of Locally Advanced Basal Cell Carcinoma: A Case Report

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ABSTRACT

Neoadjuvant Hedgehog Pathway Inhibitor (HPI) therapy, utilizing sonidegib and vismodegib, has shown great potential in managing locally advanced Basal Cell Carcinoma (laBCC). While effective, the tolerability of HPI therapy may be limited due to adverse effects (muscle spasms, alopecia). However, studies have shown a lower incidence of side effects with sonidegib, compared to vismodegib. In this report, we present the case of an 86-year-old male with laBCC on the left inner canthus treated successfully with neoadjuvant sonidegib for 25 weeks prior to Mohs micrographic surgery. This case highlights the utility of sonidegib as a potential neoadjuvant treatment modality for patients who are good candidates for surgery but would benefit from tumor reduction to achieve a more favorable outcome, especially in cosmetically sensitive areas. In addition, our patient experienced minimal side effects (muscle cramps at week 18) from sonidegib treatment.

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INTRODUCTION

Neoadjuvant Hedgehog Pathway Inhibitor (HPI) therapy, encompassing sonidegib, and vismodegib has emerged as a promising strategy in the management of locally advanced Basal Cell Carcinoma (laBCC).[1]This approach is currently indicated for adults with recurrent laBCC, patients who are not surgical or radiation candidates, and those with metastatic BCC.[1]

While HPI therapy has demonstrated its efficacy in patients with advanced BCC, its tolerability varies due to adverse effects (AE). Among the most common AEs of any grade are muscle spasms (49%), alopecia (43%), dysgeusia (38%), nausea (33%), elevated creatine kinase (CK; 29%), fatigue (29%), weight loss (27%), and diarrhea (24%).[2,3] The most serious AEs reported were elevated CK and rhabdomyolysis (1%).[4]

The BOLT study significantly solidified sonidegib's role in advanced BCC treatment, with a higher objective response rate, fewer adverse events, prolonged treatment duration, a lower discontinuation rate, and a more favorable benefit-to-risk profile at the 200 mg daily dose compared to the 800 mg dose.[5] An earlier case report also demonstrated the successful use of sonidegib in conjunction with radiation therapy for recurrent basal cell carcinoma, delivering a complete clinical response with no significant toxicities.[5]

The choice between the two available HPI therapies, vismodegib, and sonidegib, predominantly relies on expert opinion and indirect comparisons, as there are no direct head-to-head trials. Vismodegib, the first approved HPI, has a longer track record of use and more extensive supporting medical literature. Sonidegib offers a higher objective response rate, longer median progression-free survival, an extended median duration of response for laBCC, and is slightly less expensive than vismodegib.[6,7] Sonidegib is associated with the same AEs as vismodegib but exhibits a lower incidence by approximately 10%, with less severity and a slightly longer median time to onset.[8] Specifically, the median time to onset of the most frequent AEs, such as muscle spasms, alopecia, and dysgeusia, was 1 to 2 months for patients on vismodegib 150 mg daily, compared to 2 to 6 months for patients taking sonidegib 200 mg daily.[8] Nevertheless, pinpointing the subset of patients who could benefit more from one HPI over the other remains a challenge, necessitating further research to confirm the effectiveness of sonidegib in treating BCC.[8]

Case reports and clinical trials have underscored the potential of sonidegib in inducing tumor remission and its effectiveness as a neoadjuvant treatment for laBCC before Mohs surgery. In this report, we describe a case of a locally advanced basal cell carcinoma on the left inner canthus treated with neoadjuvant sonidegib prior to Mohs micrographic surgery.

CASE

An 86-year-old male with a significant cardiovascular history (congestive heart failure, atrial fibrillation, hyperlipidemia), stage 3 chronic kidney disease, and psoriasis vulgaris managed with risankizumab presented with a 2 to 3 cm pearly erythematous nodule with telangiectasias on the left inner canthus. Histopathology revealed aggregates of basaloid cells with peripheral palisading and tumor retraction, consistent with basal cell carcinoma. Given that the BCC was in a cosmetically sensitive area and near the nasolacrimal duct, several options were discussed prior to surgery, and per his preference was started on sonidegib (200 mg daily) and L-carnitine to prevent muscle cramps. After 4 weeks of treatment, the tumor flattened and decreased in size significantly to 1 to 2 cm, and with continued treatment, there was an observed 80% reduction in size by week 8.

The patient experienced no side effects from the sonidegib (muscle cramps) or worsening of his other medical conditions until week eighteen, during which he experienced tolerable mild cramps in his hands. At week 25, the size of the tumor was 1.0 x 0.8 cm, almost a 90% decrease from baseline. The basal cell carcinoma was then successfully removed with 1 stage of Mohs micrographic surgery, and the defect was reconstructed with an inferiorly-based rotation flap with preserved eyelid position and excellent cosmesis.

FIGURE 1. Locally advanced basal cell carcinoma prior to initiation of sonidegib.

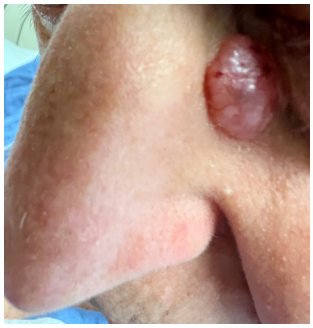


FIGURE 2. Basal cell carcinoma with 4 weeks of treatment with sonidegib.

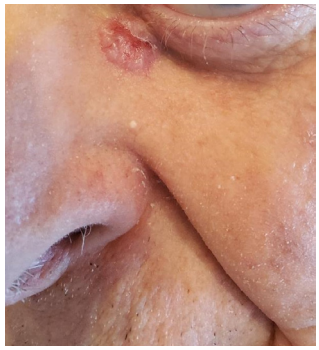


FIGURE 3. Basal cell carcinoma with 8 weeks of treatment with sonidegib

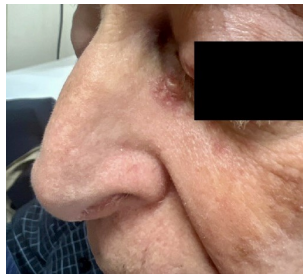


FIGURE 4. Basal cell carcinoma with 25 weeks of treatment with Sonidegib.

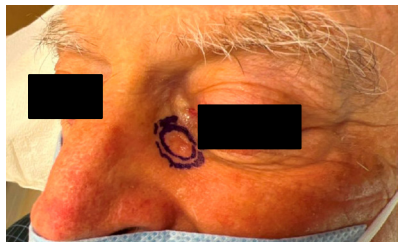
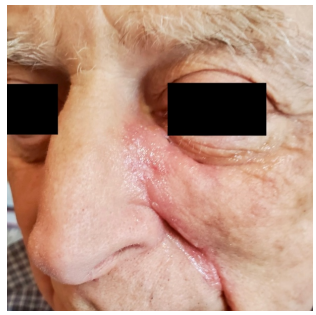


FIGURE 5. Treated basal cell carcinoma status post-four weeks after Mohs micrographic surgery and 25 weeks of sonidegib.



DISCUSSION

In this case report, we have documented the successful management of a locally advanced periorbital basal cell carcinoma using neoadjuvant sonidegib, followed by Mohs micrographic surgery. Basal cell carcinoma (BCC) may present unique challenges when they occur on functionally and cosmetically sensitive areas. Mohs micrographic surgery remains the gold standard for managing BCCs on the face.[9] However, for cases where surgical intervention may be challenging or associated with morbidity, neoadjuvant therapy may offer a benefit. Vismodegib, another Hedgehog Pathway Inhibitor (HPI), has shown efficacy in treating locally advanced BCC, but it is not without side effects.[9,10] Our patient's experience exemplifies the potential of sonidegib to reduce the size of a tumor, making surgical extirpation easier. Moreover, the treatment course was relatively uncomplicated, with only mild hand cramping after week 18.

In addition to HPI therapy, alternative neoadjuvant strategies are available for BCC, including topical imiquimod, pembrolizumab, and cemiplimab. Topical imiquimod is indicated for patients with low-risk, superficial BCC below the neck; however, its cure rates are inferior to surgery and radiation.[11] Notably, imiquimod has been employed as a neoadjuvant therapy before Mohs micrographic surgery.[11] The high tumor mutational burden of BCCs suggests that programmed cell death-ligand 1 (PD-L1) inhibitors, like pembrolizumab, may be active against advanced BCCs.[12] For patients who are refractory to or experiencing recurrence after HPI therapy, pembrolizumab, a PD-L1 inhibitor, may be used as a monotherapy or in conjunction with HPIs.[12] Furthermore, cemiplimab, a humanized monoclonal antibody against PD-1, demonstrates potential in the treatment of BCC, with an overall response rate of 78% and a disease control rate of 100%.[13] It represents a therapeutic alternative for locally advanced or metastatic BCCs that fail to respond to or recur after HPI treatment.[13]

CONCLUSION

This case underscores the importance of individualized treatment approaches, considering both the patient's health, treatment goals and the characteristics of the tumor. While more research is needed to further validate sonidegib's efficacy as a neoadjuvant therapy for locally advanced BCCs, this case offers evidence of the potential benefits of this approach. As the field of cutaneous oncology continues to evolve, it is essential to explore and optimize diverse treatment strategies to provide the best possible outcomes for patients.

DISCLOSURES

Authors Hollield and Amara do not have any conflicts of interest to disclose. Author Lewin is an employee of Mount Sinai and does not have any conflicts of interest to disclose. Mark Lebwohl is an employee of Mount Sinai and receives research funds from: Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Janssen Research & Development, LLC, Ortho Dermatologics, Pfizer, Sanofi-Regeneron, and UCB, Inc., and is a consultant for Almirall, AltruBio Inc., AnaptysBio, Apogee, Arcutis, Inc., AstraZeneca, Atomwise, Avotres Therapeutics, Brickell Biotech, Boehringer-Ingelheim, Bristol-Myers Squibb Castle Biosciences, Celltrion, Corevitas, Dermavant Sciences, EPI, Evommune, Inc., Facilitation of International Dermatology Education, Forte biosciences, Foundation for Research and Education in Dermatology, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi-Regeneron, Seanergy, Strata, Takeda, Trevi, and Verrica.

Ethical statement: Our unidentifiable patient gave consent for publication.

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