### **Understanding Vismodegib and Sonidegib: For Patients**

Zaim Haq

# What are Vismodegib and Sonidegib?

Vismodegib is a medication known as a "sonic hedgehog inhibitor." It's specifically used to treat certain types of skin cancer, primarily basal cell carcinoma (BCC), which is the most common form of skin cancer worldwide. Doctors prescribe vismodegib when surgery or radiation are either not suitable or effective, such as when cancer has spread or returned multiple times<sup>1</sup>.

Besides vismodegib, another similar medication called sonidegib is also approved for treating advanced BCC. Like vismodegib, sonidegib works by targeting the Sonic Hedgehog pathway. Choosing between them depends on your situation, side-effect tolerance, and your doctor's recommendation<sup>1</sup>.

# How Do "Sonic Hedgehog Inhibitors" Work?

Vismodegib and other sonic hedgehog inhibitors target a biological pathway in cells called the "sonic hedgehog signaling pathway." Normally, this pathway helps control how cells grow and divide. However, in BCC, mutations can cause this pathway to become overactive, leading to uncontrolled growth of cancer cells<sup>1</sup>.

Vismodegib and other sonic hedgehog inhibitors block this pathway by inhibiting a protein called Smoothened (SMO). By stopping SMO, they prevent cancer cells from growing and dividing, ultimately shrinking or controlling the tumor<sup>1</sup>.

### Effectiveness of Sonic Hedgehog Inhibitors

In recent years, there have been several clinical studies that have shown promising results for vismodegib. In one clinical study consisting of 104 patients, nearly 45% of patients with metastatic BCC experienced significant tumor shrinkage<sup>2</sup>. In another study of patients treated with vismodegib, 30% of patients with metastatic basal cell carcinoma had tumor shrinkage, and 43% of patients with locally advanced basal cell carcinoma responded to treatment, including complete tumor clearance in 21% of these patients<sup>3</sup>.

#### Possible Side Effects

Like many cancer treatments, vismodegib has potential side effects. Common symptoms for patients on this medication include:

- Muscle cramps
- Hair loss

- Changes in taste or loss of taste
- Weight loss
- Fatigue
- Nausea
- Diarrhea

Most side effects improve once the treatment stops, but it's important to discuss these thoroughly with your physician to manage them effectively. Additionally, some tumors might develop resistance over time, causing the medication to lose effectiveness in certain cases<sup>1, 2, 4</sup>.

## Who Should Consider Sonic Hedgehog Inhibitors?

Vismodegib isn't for everyone with BCC. Doctors typically recommend it for patients with advanced or metastatic BCC where surgery or radiation isn't effective or for people who have had multiple recurrences of BCC. Vismodegib may also be prescribed in situations where the tumor's location may result in difficulty with surgical removal<sup>1</sup>.

In most cases, your doctor will discuss with you if vismodegib is the right treatment based on your situation and medical history. If you're prescribed vismodegib, you'll regularly see your doctor for check-ups. These visits include monitoring the tumor size, assessing side effects, and adjusting your treatment plan as needed. Regular follow-ups are important to manage side effects and check your progress.

Vismodegib and other sonic hedgehog inhibitors offer important treatment options for patients with advanced BCC, especially when traditional methods aren't enough. By understanding how these treatments work and their side effects, you can better manage your health and make informed decisions alongside your healthcare team.

- Dummer R, Ascierto PA, Basset-Seguin N, Dréno B, Garbe C, Gutzmer R, Hauschild A, Krattinger R, Lear JT, Malvehy J, Schadendorf D, Grob JJ. Sonidegib and vismodegib in the treatment of patients with locally advanced basal cell carcinoma: a joint expert opinion. J Eur Acad Dermatol Venereol. 2020 Sep;34(9):1944-1956. doi: 10.1111/jdv.16230. Epub 2020 Mar 4. PMID: 31990414.
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- 3. Sekulic A, Migden MR, Basset-Seguin N, Garbe C, Gesierich A, Lao CD, Miller C, Mortier L, Murrell DF, Hamid O, Quevedo JF, Hou J, McKenna E, Dimier N, Williams S, Schadendorf D, Hauschild A; ERIVANCE BCC Investigators. Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. BMC Cancer. 2017 May 16;17(1):332. doi:

- 10.1186/s12885-017-3286-5. Erratum in: BMC Cancer. 2019 Apr 18;19(1):366. doi: 10.1186/s12885-019-5568-6. PMID: 28511673; PMCID: PMC5433030.
- 4. Sinx KAE, Roemen GMJM, van Zutven V, Janssen R, Speel EM, Steijlen PM, van Geel M, Mosterd K. Vismodegib-resistant basal cell carcinomas in basal cell nevus syndrome: Clinical approach and genetic analysis. JAAD Case Rep. 2018 Apr 30;4(5):408-411. doi: 10.1016/j.jdcr.2017.11.011. PMID: 29984265; PMCID: PMC6031482.

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