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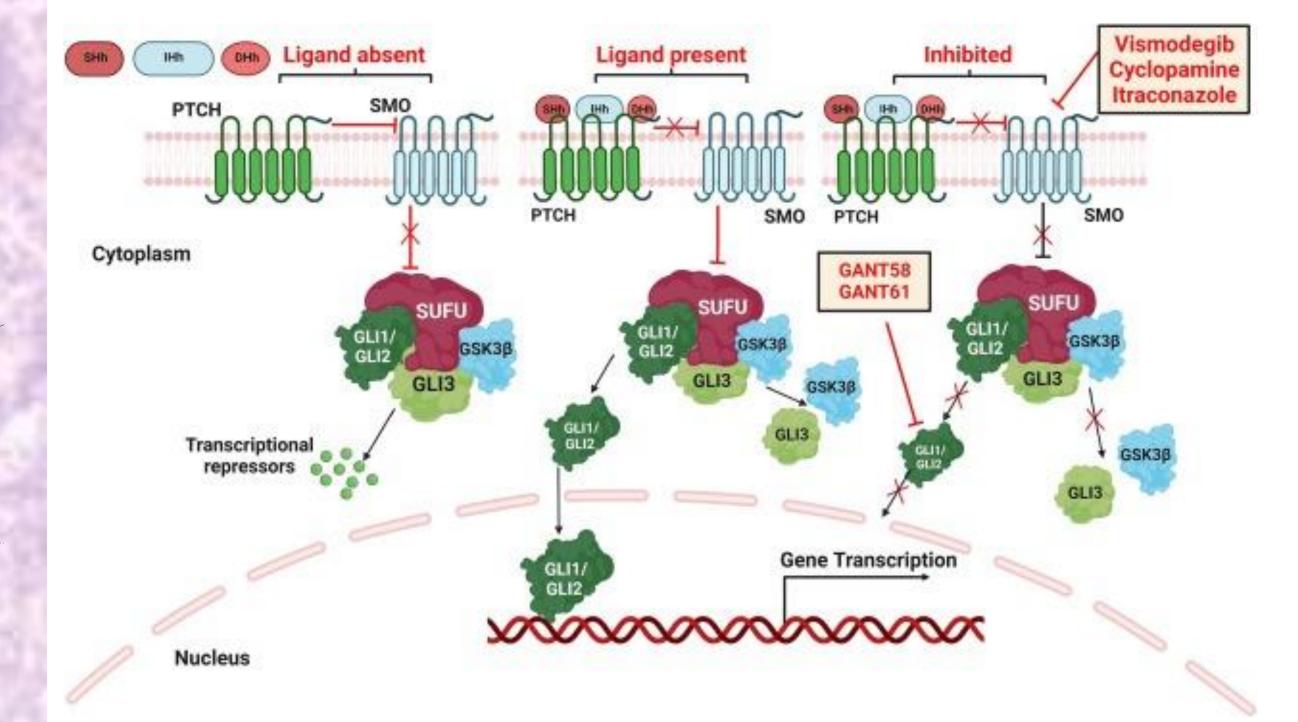
Hedgehog pathway inhibitors in basal cell carcinoma: real-life experience

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BACKGROUND AND IMPORTANCE

Basal cell carcinoma (BCC) is the most common skin cancer, with advanced cases often difficult to treat using traditional methods like surgery and radiotherapy.



The Hedgehog signaling pathway plays a key role in BCC, leading to treatments like vismodegib and sonidegib. This study evaluates their effectiveness and safety in real clinical settings.

> Wen J, Hadden MK. Medulloblastoma drugs in development: Current leads, trials and drawbacks. Eur J Med Chem. 2021 Apr 5;215:113268. doi: 10.1016/j.ejmech.2021.113268. Epub 2021 Feb 8. PMID: 33636537; PMCID: PMC8009859.

OBJETIVE

The study aims to evaluate the effectiveness and safety of Hedgehog pathway inhibitors in patients with locally advanced or metastatic basal cell carcinoma. It focuses on treatment response, tumor recurrence, and adverse events, while comparing outcomes between vismodegib and sonidegib, two commonly used inhibitors in clinical practice.

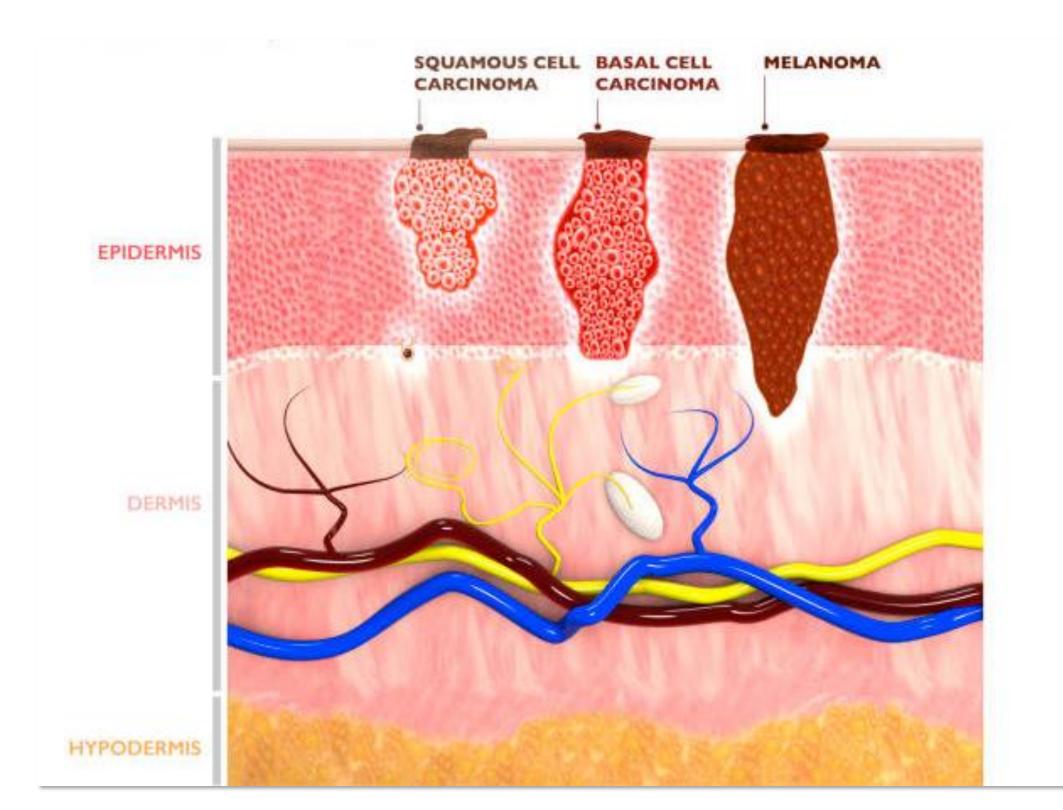
METHODS AND MATERIAL

A retrospective observational study was conducted on patients with locally advanced or metastatic basal cell carcinoma between December 2020 and March 2024. Data on demographics, tumor location, treatment details, and adverse events were collected. Patients received vismodegib or sonidegib, with treatment effectiveness assessed by disease recurrence. Quality of life was measured using the ECOG scale. Adverse events, dose modifications, and reasons for treatment discontinuation were also recorded. In some cases, neoadjuvant treatments were used to facilitate subsequent surgeries.

RESULTS

The study included 14 patients, of whom 64.29% were male and the mean age was 76.21 years. Most of the patients (57.14%) received off-label neoadjuvant treatment, and the rest were cases of inoperable locally advanced BCC. The tumors were predominantly located on the face (64.29% of cases).

All patients treated with sonidegib had adverse events (ADRs), including hematologic toxicity and muscle damage, leading to discontinuation or dose adjustment in some cases. Adverse events were also experienced by 77.78% of vismodegib-treated patients. There was tumor recurrence in 25% of neoadjuvant-treated patients. Three patients treated with vismodegib were able to maintain response after more than 12 months, and four other patients with inoperable BCCla remain on treatment with significant tumor regression.



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CONCLUSIONS



Hedgehog pathway inhibitors, vismodegib and sonidegib, effectively treat locally advanced and metastatic BCC, offering an alternative to surgery or radiotherapy. Despite frequent adverse effects, they control disease and enable salvage surgeries. Further research is needed to compare effectiveness, manage side effects, and improve treatment adherence.

