

ADVANCED BASAL CELL CARCINOMA:

HOW TO NAVIGATE
CHALLENGING
CLINICAL SCENARIOS
WITH SYSTEMIC
TREATMENT

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ANNENBERG CENTER FOR HEALTH SCIENCES

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As in medicine generally, the management of patients with locally advanced basal cell carcinoma is rapidly evolving. To help clinicians keep abreast of new information, this CME activity will be updated 4 times through October 2021. This first update includes new information released between February 17, 2021, and April 7, 2021.



Efficacy of sonidegib in histologic subtypes of advanced basal cell carcinoma: Results from the final analysis of the randomized phase 2 Basal Cell Carcinoma Outcomes With LDE225 Treatment (BOLT) trial at 42 months.

Dummer R, et al. *J Am Acad Dermatol*. 2021;84(4):1162-1164.



Sonidegib: BOLT Trial at 42 Months

- 42-month follow-up of the BOLT trial provided results similar to those observed at 6 and 30 months.
- Objective response rates (ORRs) at 42 months:
 - Locally advanced basal cell carcinoma
 - Sonidegib 200 mg
 - Aggressive: 59.5%
 - Non-aggressive: 51.7%
 - Sonidegib 800 mg*
 - Aggressive: 45.3%
 - Nonaggressive: 47.2%
 - Highest ORRs in sonidegib 200 mg group were in infiltrative and morpheaform aggressive subtypes

*Investigational/dose not approved in United States



A review of hedgehog inhibitors sonidegib and vismodegib for treatment of advanced basal cell carcinoma.

Migden M, et al. *J Drugs Dermatol*. 2021;20(2):156-165.



Efficacy, Safety, and Pharmacokinetics of Sonidegib and Vismodegib

- Review of efficacy, safety, and pharmacokinetics of sonidegib and vismodegib based on BOLT (sonidegib) and ERIVANCE, STEVIE, and MIKIE (vismodegib) trials.
- In locally advanced basal cell carcinoma
 - Objective response rates
 - Sonidegib: 46% to 71%
 - Vismodegib: 60% to 69%
 - Progression-free survival
 - Sonidegib: 19 to 25 months
 - Vismodegib: 13 to 23 months
 - Similar efficacy for sonidegib and vismodegib by histologic tumor subtype



Efficacy, Safety, and Pharmacokinetics of Sonidegib and Vismodegib (*continued*)

- Comparable safety profiles for sonidegib and vismodegib with muscle spasms, alopecia, and dysgeusia the most common grade ≤ 2 adverse events
 - Similar findings for vismodegib for age ≥ 65 years vs < 65 years
- Pharmacokinetics
 - Sonidegib: peak plasma concentration in 2-4 hours; steady state by week 17
 - Vismodegib: peak plasma concentration in 2 days; steady state within 21 days



Predictive factors of non-response to vismodegib in locally advanced basal-cell carcinoma.

Marecassier H, et al. *Dermatology*. 2021;doi:10.1159/000512889.



Vismodegib: Predictive Factors for Tumor Response

- Retrospective review of consecutive patients treated with vismodegib for locally advanced basal cell carcinoma (N=83)
- Tumor response for target lesions was assessed using RECIST 1.1 criteria as complete response, partial response, progressive disease, or stable disease
- Two main tumor subtypes were identified, infiltrative (61.5%) and morpheaform (26.6%)
- Mean duration of follow-up for patients treated with vismodegib was 9.7 months



Vismodegib: Predictive Factors for Tumor Response (*continued*)

- 58 were responders and 25 nonresponders
- History of prior treatment with radiotherapy, presence of muscle involvement, and intermittent treatment with vismodegib were significantly associated with nonresponse
- No statistically significant difference between the responders and nonresponders regarding WHO performance status, gender, age, body mass index, or comorbidities



Other Publications

- Gershoni A, et al. Vismodegib improves quality of life in patients with periocular locally advanced basal cell carcinoma: subgroup analysis, STEVIE trial. *Eye (Lond)*. 2021;doi:10.1038/s41433-021-01493-2.
- Habashy S, et al. Hedgehog pathway inhibitors: Clinical implications and resistance in the treatment of basal cell carcinoma. *Cureus*. 2021;13(3):e13859.
- Moscarella E, et al. Management of advanced basal cell carcinoma: Real-life data with sonidegib. *Dermatol Ther*. 2021;e14948.
- The N, et al. The role of actin in muscle spasms in a case series of patients with advanced basal cell carcinoma treated with a hedgehog pathway inhibitor. *Dermatol Ther (Heidelb)*. 2021;11(1):293-299.
- Verkouteren BJA, et al. Eight years of experience with vismodegib for advance and multiple basal cell carcinoma patients in the Netherlands: a retrospective cohort study. *Br J Cancer*. 2021;124(7):1199-1206.
- Villani A, et al. Dose reduction during routine treatment of locally advanced basal cell carcinoma with the hedgehog inhibitor sonidegib to manage adverse effects: A retrospective care series. *J Am Acad Dermatol*. 2021;84(4):e211-e212.

