

# ADVANCED BASAL CELL CARCINOMA:

HOW TO NAVIGATE  
CHALLENGING  
CLINICAL SCENARIOS  
WITH SYSTEMIC  
TREATMENT

Update #1: April 2021



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  $\leq 2$  adverse events
  - Similar findings for vismodegib for age  $\geq 65$  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.

