Response to "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"

To the Editor: Basal cell carcinoma (BCC) constitutes approximately 80% of nonmelanoma skin cancers. Tumor size, location, histologic characteristics, margins, and recurrence rates are the most commonly used prognostic factors to classify BCCs. The most common histologic subtypes of BCC are the nonaggressive ones (nodular and superficial), followed by morpheaform, infiltrative, micronodular, and basosquamous, which are considered to be the most aggressive forms.[1,2] Although surgical excision is the treatment of choice for the majority of BCCs, alternative treatments using targeted therapy to inhibit the Hedgehog signaling pathway have been recently developed to treat invasive forms. In particular, sonidegib has been approved for patients aged ≥18 years with locally advanced BCC who are ineligible for surgery or radiotherapy or who present with recurrence following these treatment strategies.[3]

We read with great interest the article recently written by Dummer et al[4] regarding the long-term efficacy of sonidegib 200 and 800 mg once daily for different histologic subtypes of BCC at 42 months and we also want to report our preliminary results based on our real-life experience. A single-center, retrospective clinical study was conducted at the Nonmelanoma Skin Cancer Unit of the University of Federico II, Naples. All patients provided written informed consent. Inclusion criteria included patients >18 years with one target lesion that was a locally advanced BCC (tumor diameter, ≥10 mm, was recurrent, surgical resection would result in substantial deformity, or the tumor was deemed inappropriate for radiation therapy), and receiving sonidegib 200 mg orally daily for up to 24 weeks. Patients with metastatic BCC, or who were pregnant or breastfeeding, were excluded from the study. The primary endpoint was to assess sonidegib efficacy across BCC histologic subtypes by evaluating the tumor response rate. Clinical responses were divided into: a) complete response (disappearance of palpable or visible tumor); b) partial response (>50% tumor reduction); c) stable disease (≤50% tumor reduction, or <20% increase in tumor area); or d) progressive disease (≥20% increase in tumor area). Tumor evaluations were conducted at baseline and every 4 weeks thereafter. A total of 18 patients (16 males [88.9%] and 2 females [11.1%]; median age, 77.8 years) with locally advanced BCC (aggressive, 11 of 18 [61.1%]; nonaggressive, 7 of 18 [38.9%]) were included in the study. None of the patients had basal cell nevus syndrome. All patients completed 24 weeks of sonidegib treatment and the following tumor response rates were achieved; 12 patients (66.6%) achieved complete response, 4 patients (22.2%) achieved partial response, and 2 patients (11.2%) achieved stable disease (Table I). None of the patients presented with progressive disease. The highest rates of complete response were found in aggressive tumor subtypes (8 of 11 [72.7%]). Approximately 50% of patients with nonaggressive subtypes in each group achieved complete response. All BCC histopathologic subtypes showed similar histopathologic clearance over 24 weeks of treatment, with no significant differences reported according to the histological subtype. Interestingly, a trend of increased clearance of infiltrative tumors after 12 weeks of treatment was observed.

Table I. Overall response in patients with aggressive and nonaggressive subtypes of advanced basal cell carcinoma after 24 weeks of 200 mg sonidegib treatment

	Aggressive		Nonaggressive	
Best overall response	**Infiltrative (n = 9)**	**Morpheaform (n = 2)**	**Nodular (n = 4)**	**Superficial (n = 3)**
Complete response	7 (77.7%)	1 (50%)	2 (50%)	2 (66.7%)
Partial response	1 (11.15%)	1 (50%)	1 (25%)	1 (33.3%)
Stable disease	1 (11.15%)	0	1 (25%)	0
Progressive disease	0	0	0	0
Overall response rate*	8 (88.85%)	2 (100%)	3 (75%)	3 (100%)

Data are shown as number (%).
*Calculated as Complete response + Partial response.

The limitations of this study include the small sample size. These are preliminary results. Only patients who completed 24 weeks of sonidegib treatment were included in the study and data including long-term follow-up responses are needed.

Alessia Villani, MD, Gabriella Fabbrocini, PhD, Claudia Costa, MD, and Massimiliano Scalvenzi, PhD

From the Dermatology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy.

Funding sources: None.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Alessia Villani, MD, Dermatology Unit, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

E-mail: ali.vil@hotmail.it

Conflicts of interest

None disclosed.

REFERENCES

1. Mohan SV, Chang ALS. Advanced basal cell carcinoma: epidemiology and therapeutic innovations. *Curr Dermatol Rep*. 2014;3(1):40-45.
2. Marzuka AG, Book SE. Basal cell carcinoma: pathogenesis, epidemiology, clinical features, diagnosis, histopathology, and management. *Yale J Biol Med*. 2015;88(2):167-179.
3. Villani A, Fabbrocini G, Costa C, Scalvenzi M. Sonidegib: safety and efficacy in treatment of advanced basal cell carcinoma. *Dermatol Ther (Heidelb)*. 2020;10(3):401-412.
4. Dummer R, Lear JT, Guminski A, Leow LJ, Squittieri N, Migden M. 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. *J Am Acad Dermatol*. 2020;84(4):1162-1164.

https://doi.org/10.1016/j.jaad.2021.02.074