

# Systemic hedgehog inhibitors to treat locally advanced basal cell carcinomas of the head–neck region: A retrospective study

Dear Editor,

Basal cell carcinoma (BCC) is the most commonly diagnosed human cancer, typically occurring in fair-skinned subjects over 50 years old. Although it could occur in multiple locations, 80% of the patients present advanced BCCs of the head–neck region usually causing functional and cosmetic problems. Standard excision and Mohs surgery are the gold-standard treatment for the majority of BCCs, even if topical treatment, including 5-fluorouracil and imiquimod, photodynamic therapy, cryotherapy, or curettage could also be considered for selected low-risk BCCs. In some they can progress to an advanced stage invading the surrounding structures locally or metastasizing, resulting in locally advanced (la) and metastatic (m) BCCs, respectively. In the majority of cases, these advanced tumors cause morbidity due to their proximity to critical facial structures resulting in disfigurement and lowering patients' quality of life (QoL).<sup>1,2</sup> Advanced BCCs are not always candidates for surgery or radiation therapy, thus requiring alternative treatments.<sup>3,4</sup> Sonidegib, is a selective hedgehog pathway inhibitor (HHI) approved in 2015 for patients with laBCC that are ineligible for surgery and/or radiation therapy.<sup>5</sup> To date, clinical trials and case reports regarding its efficacy and tolerability, also during COVID-19 pandemic period,<sup>6</sup> have already been reported<sup>7,8</sup>; the aim of this study is to report the efficacy of sonidegib in treating laBCCs localized in critical structures as the head–neck region, highlighting also the cosmetic results reported in patients achieving the complete remission of the tumor. This retrospective analysis included patients with head–neck laBCCs treated with sonidegib at the Non-Melanoma Skin Cancer Unit of the University of Federico II in Naples from February 2020 to December 2020. Only patients receiving at least 24 weeks of sonidegib treatment were included in the study. Baseline data included sex, age, area, primary tumor or recurrence and orbital involvement. Therapeutic response, measuring the extent of the tumor was divided in complete remission (CR), partial remission (PR; > 50% of tumor regression), stable disease (SD; < 50% of tumor regression), and progressive disease (PD; for patients with >20% of tumor increase). Adverse events were also collected. Data are reported in Table 1. Thirteen patients (11 males and 2 females) with a median age of 77.8 (range 52–95) years were treated with sonidegib at the approved dosage of 200 mg/daily. Median duration of sonidegib treatment was 6.5 months (range 6–9 months). Four out of

13 patients had disease localized on the temple region, 4 out of 13 on the ocular and periocular region, 2 out of 13 on the zygomatic region, 2 out of 13 patients had laBCC of the nose and 1 patient had laBCC of the nuchal region. All BCC were histologically confirmed. At treatment end, 6 (46.1%) patients were considered with CR, 4 (30.7%) with PR, 1 (7.6%) with SD and 2 (15.6%) patients discontinued treatment due to multiple adverse events (AEs). Overall, 10 out of 13 patients (76.9%) reported more than one AE related to the drug. Our retrospective analysis confirmed the efficacy of sonidegib in treating advanced BCCs, reporting an objective response rate (ORR: CR + PR) in 10 (76.8%) patients; moreover, in all patients presenting the tumor in difficult-to-treat areas good cosmetic results were obtained. Although surgery still represents the gold-standard treatment for the majority of BCCs, for the advanced ones, the use of HHI

**TABLE 1** Patient demographic and clinical characteristics (n = 13)

	laBCC (n = 13)
Median age, years (range)	77.8 (52–95)
Gender, % (n)	
Male	84.6 (11)
Female	15.4 (2)
Primary site of tumor, % (n)	
Templar region	30.7 (4)
Ocular region	30.7 (4)
Zygomatic region	15.4 (2)
Nasal region	15.4 (2)
Nuchal region	7.8 (1)
Median duration of treatment	6.5 months (range 6–9 months)
Response rate (%; n)	
CR	46.1 (6)
PR	30.7 (4)
SD	7.6 (1)
PD	–

Abbreviations: CR, complete remission; laBCC, locally advanced basal cell carcinoma; PR, partial remission; PD, progressive disease; SD, stable disease.

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could be also considered as neoadjuvant treatment before surgery in order to obtain better results, thus increasing patients' QoL.<sup>9,10</sup> Studies on larger sample size, reporting the use of HHI used either alone or neoadjuvantly in order to decrease tumor size before excision, ensuring tumor clearance and improving functional outcome and cosmesis, are required.

#### AUTHOR CONTRIBUTIONS

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author.

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