Locally advanced basosquamous carcinoma: Our experience with sonidegib

Dear Editor,

Basosquamous carcinoma (BSC) is a rare cutaneous tumor that presents an aggressive local growth pattern and an increased potential for recurrence and metastases. Histologically it consists of basal cell carcinoma (BCC) and areas of squamous differentiation usually with a transition zone between them.[1]

When BSC becomes locally advanced or metastatic, not amenable to surgery or radiation therapy, the therapeutic options are limited and can include the hedgehog signaling inhibitors (HHIs).

There are only a few cases in the literature of locally advanced BSCs completely treated with vismodegib[2,3] and no cases with sonidegib.

A 59-year-old woman consulted our department for a large ulcerated lesion extended from the left upper limb to the pectoral region. She was otherwise healthy, from the exception of mild anemia with thalassemic trait.

A total-body computed tomography (CT) scan revealed in the shoulder area a 10x15 cm mass infiltrating the subcutaneous tissue, deltoid muscle, pectoralis major muscle and in close contact with the cephalic vein and humerus bone. The histopathology report showed an invasive BCC with areas of squamous differentiation.

The surgery and radiotherapy were not considered feasible. After discussing with the patient the uncertain role of sonidegib in this type of tumor and the possible adverse effects (AEs), the mutual decision was to initiate sonidegib at standard dose of 200 mg daily. After 4 months, we achieved more than 50% tumor reduction without any AEs. Monthly laboratory exams showed anemia (stable values) and a slight increase of alkaline phosphatase value. The therapy will administered until disease progression or unacceptable toxicity.

In another case, an 83-year-old woman with a previous excision of ulcerated BCC of the left shoulder, was referred to our department

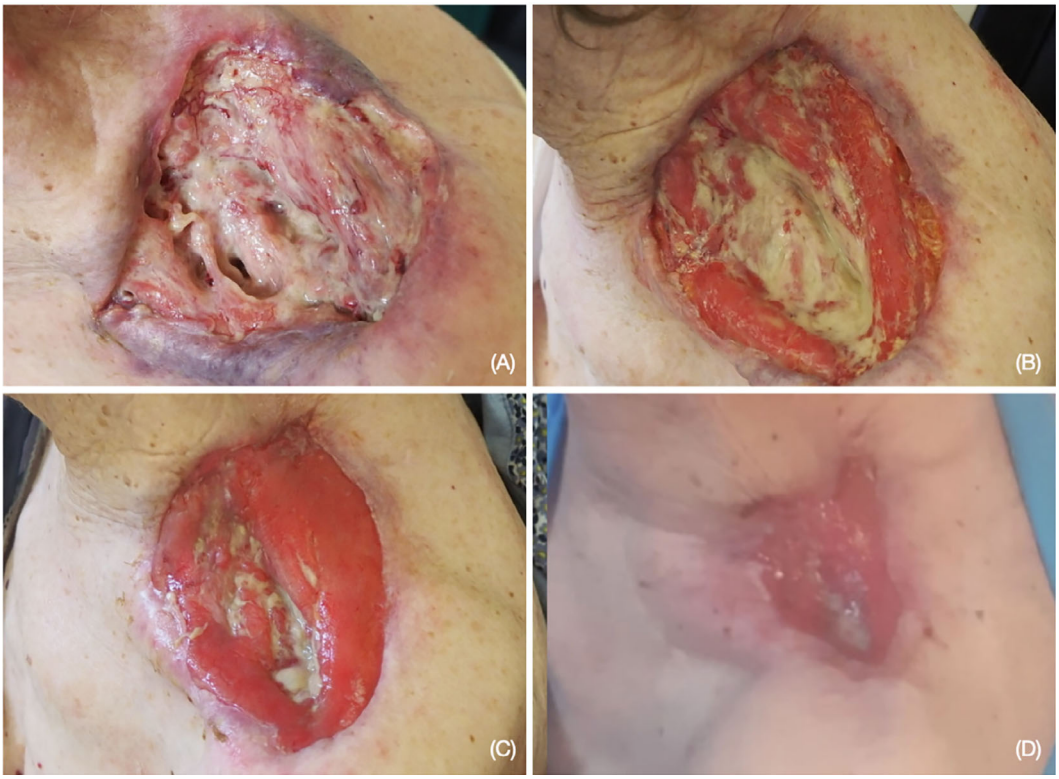

FIGURE 1 (A) Locally advanced basosquamous carcinoma of the left shoulder (case 2) treated with sonidegib. (B) Initial response of the lesion 2 months after starting therapy. (C) Partial response of the tumor after 3 months of therapy, (D) with an almost complete response 6 months after starting sonidegib

for the presence of a large ulcerated lesion, approximately 15 cm, located in left shoulder. She suffered from heart disease and arterial hypertension and reported a slow-growing subcutaneous nodule in the last 4 years, with subsequent ulceration and increase in size in recent months. The histopathology report revealed a sclerodermiform BCC with squamous metaplasia.

A magnetic resonance imaging (MRI) of the shoulder and neck area showed a huge solid mass without a cleavage plane between tumor and the surrounding soft tissue.

Surgery and radiotherapy were only possible in a palliative setting, therefore we decided to start a systemic treatment with sonidegib (200 mg/day). Three months later, a remarkable reduction, more than 50% of tumor size, was observed with an almost complete response after 6 months (Figure 1). She complained nausea, loss of appetite, myalgia, and bone pain approximately 3 months after starting therapy, with normal laboratory tests. The treatment was interrupted with partial resolution of the symptoms and after 2 weeks, sonidegib was restarted at a dosage of 200 mg every other day. The patient is still on alternate-day dosing therapy.

Currently, there are controversial results from studies investigating the potential association between vismodegib and the increased risk of squamous cell carcinoma (SCC). In fact, reports regarding the appearance of SCCs during vismodegib therapy have been published,[4] even if other papers concluded that the existing evidences does not justify this association. Despite the presence of the squamous component, few case reports of laBSCs completely treated with vismodegib have been reported.[2,3]

Sonidegib was introduced later to the market and approved for laBCC. In literature, no data of increased risk of SCCs during this HHI has been found. The significant outcome of our patients provide preliminary evidence that sonidegib might be effective for laBSC. No similar reports have been published to date.

In addition, the tumor-infiltrating T cells after administration of HHI and the high genetic mutational burden in BCC may indicate a change in immune susceptibility of the tumor and a potential benefit from checkpoint inhibitor treatment.[5] Cemiplimab, the human monoclonal antibody directed against the programmed-cell death receptor (PD)-1 and approved for the treatment of patients with advanced-stage cutaneous SCC not amenable for curative surgery or curative radiation,[6] has recently shown promising antitumour activity and a good safety profile for patients with advanced BCC who have progressed on or are intolerant to a hedgehog pathway inhibitor. In this setting cemiplimab might be a valid therapeutic option also for advanced BSC, but further studies are needed. Written informed consent was obtained from the patient for the use of image and publication of his case details.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

All authors have made substantial contributions to the work reported in the manuscript. Iris Zalaudek, Nicola di Meo, Claudio Conforti and Ludovica Toffoli conceived of the presented case report. Claudio Conforti and Ludovica Toffoli wrote the manuscript. Iris Zalaudek, Marina Agozzino, Claudio Conforti and Ludovica Toffoli contributed to the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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