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LETTER

Sonidegib-induced muscle spasms in the treatment of basal cell carcinoma: Strategies to adopt

Dear Editor,

We read with great interest the article written by *Trabelsi* et al.[1] regarding the management of sonidegib treatment in multiple basal cell carcinomas during COVID-19 pandemic period and we also want to report our experience. Sonidegib is a hedgehog pathway inhibitor (HPI) approved for the treatment of patients with locally advanced basal cell carcinoma (laBCC). From 95% to 100% of patients treated with hedgehog pathway inhibitors, experience at least one treatment-related adverse event (AE) with "muscle spasms" being AE most frequently observed.[2] In the 42-month analysis of the phase II, randomized BOLT study muscle spasms were reported in 54% of patients treated with 200 mg sonidegib (for a median duration of 11 months), leading to treatment discontinuation in 5% of cases.[3] Adequate hydration, physical activity, and several pharmacological treatments have been recommended in order to better manage muscle spasms; moreover creatine-kinase levels have to be tested every month in patients undergoing sonidegib treatment.[4] Aim of this single-center analysis was to retrospectively review and assess the occurrence of muscle spasms and describe their management in all patients with laBCC treated with 200 mg sonidegib (from February 2020 to August 2021) during COVID-19 pandemic period. 62 patients (44 males and 18 females) with a median age of 75.8 years were included in the study. The median duration of treatment with sonidegib was 7.6 months. 49 out of 62 (79%) patients experienced muscle spasms with 43 patients (88%) with grade I–II of severity and 6 patients (12%) with grade III of severity, according to Common Terminology Criteria for Adverse Events.[5] The majority of AEs reported were mild or moderate, occurring early in the course of treatment. Reported rate of discontinuation because of all AEs during the year following the initiation was 39% (24/62 patients), in particular, 4 of them (16.6%) for muscle spasms, 14 patients (54.1%) stopped treatment for multiple AEs and 6 patients (29.3%) discontinued treatment following "their own judgment." Muscle spasms appeared, on average, 1.8 months after treatment initiation affecting lower limbs and foot (73%) and upper limbs (67%); they usually occurred at night (83%), at rest (53%), affecting patients' daily activities. 64% among patients affected presented muscle spasms every day, whereas, 36% several times during a week. Several strategies were adopted during treatment in order to correct manage the AE, improving patients' quality of life. 21 out of 49 patients (43%) presenting muscle spasms were prescribed magnesium supplementation, 16 patients (33%) received the alternate dosing regimen (200 mg sonidegib every other day) and 12 patients were prescribed gabapentin (100 or 200 mg daily according to the grade of severity). The majority of patients referred general improvement with 78% having a grade decrease from III to II or II to I (Table 1). Adopting correct strategies to manage muscle spasms resulted reducing the toxicity, thus preventing treatment discontinuation in elderly patients, also considering the possible rate of treatment discontinuation during the pandemic period. In literature there are no many data regarding real-life experiences on the AEs related to HPI treatment[6,7]; our retrospective study showed that although muscle spasms represent a common AE arising in patients undergoing hedgehog pathway inhibitors, they usually occur in a mild–moderate grade; the reduction of dosing regimen and/or the supplementation with non-pharmacological and pharmacological therapies could be useful strategies to prevent drug-induced toxicity. Further studies are still required.

TABLE 1 Characteristics of study population

Males:Females	42:18
Median age (years)	75.8
Median duration of treatment (months)	7.6
N. patients experiencing muscle spasms (*n*; %)	49; 79% 43 grade I–II 6 grade III
Rate of treatment discontinuation (*n*; %)	24; 39%
Medium time of onset of muscle spasms (months)	1.8 months

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed equally to the manuscript.

ETHICS STATEMENT

Approval of ethical committee was obtained from the University Federico II of Naples, Italy.

DATA AVAILABILITY STATEMENT

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

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