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from Bristol-Myers Squibb, Novartis, Pierre-Fabre, Sun Pharmaceutical, Sanofi-Regeneron, Amgen, Merck-Serono, and Merck Sharp & Dohme. **NS** is an employee of Sun Pharmaceutical Industries, Inc. **RA** and **JD** are employees of Sun Pharmaceutical Industries, (Europe) B.V. **BD** has been a consultant or advisor for Bristol-Myers Squibb, GlaxoSmithKline, Roche, and Novartis; has served on speakers’ bureaus for Bristol-Myers Squibb, GlaxoSmithKline, and Roche; has received research funding from Amgen, Bristol-Myers Squibb, and GlaxoSmithKline; and has received travel support from Bristol-Myers Squibb and Roche.

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Basal cell carcinoma (BCC) is the most common US skin malignancy, and its European incidence is increasing.¹ Patients with locally advanced (laBCC) or metastatic BCC (mBCC) require treatment options other than traditional surgery and radiation, which can produce scarring and disfigurement that cause psychological stress.² Sonidegib is a Hedgehog pathway inhibitor approved to treat advanced BCC (aBCC; Switzerland and Australia) and laBCC (US and EU).³ ⁴ Limited data exist regarding quality of life (QoL) in patients with aBCC.² Assessments of QoL in patients with laBCC and mBCC were conducted during the Basal Cell Carcinoma Outcomes with LDE225 Treatment (BOLT) trial for sonidegib.

BOLT was a multicenter, randomized, double-blind, phase 2 study evaluating efficacy and safety of sonidegib (200 and 800 mg) in patients with laBCC or mBCC not amenable to surgery or radiation therapy, and has been described.⁵ All patients were invited to complete the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) and associated Head and Neck Cancer Module 35 (H&N35) at baseline, Weeks 9 and 17, every 8 weeks (first year), and then every 12 weeks until end of treatment (EOT). QLQ-C30 and H&N35 subscales most applicable to patients with aBCC were evaluated, including physical functioning, social functioning, pain, and fatigue (QLQ-C30), and trouble with social contact, weight loss, and head and neck pain (H&N35). Higher functioning subscale scores indicated positive (improved) change with high function, while higher symptom subscale scores indicated negative (worsened) change with high levels of symptoms. Analyses included mean change from baseline in subscale scores over time.

This study was conducted according to the ethical principles of the Declaration of Helsinki with approvals from local ethics committees or Institutional Review Boards. All patients provided informed consent.
Sixty-six patients with laBCC and 13 with mBCC received the approved sonidegib 200 mg daily dose. Median duration of exposure was 8.9 months; 91% of patients received treatment for ≥4 months. Overall, 88.7% (QLQ-C30) and 90.0% (H&N35) of all patients had baseline and ≥1 postbaseline questionnaire assessment. Mean changes from baseline scores for QLQ-C30 and H&N35 subscales were generally modest, and positive and negative fluctuations appeared evenly distributed for most subscales (Figures 1 and 2; Supplemental Tables 1 and 2).

**Figure 1.** Mean change from baseline* in EORTC QLQ-C30 subscale† scores over time

*Mean baseline scores ± SD were 81.26 ± 22.39, 88.51 ± 18.49, 18.24 ± 24.23, and 21.70 ± 20.36 for physical functioning, social functioning, pain, and fatigue subscales, respectively.

†Higher scores on physical functioning and social functioning subscales indicated positive (improved) change, while higher scores in pain and fatigue subscales indicated negative (worsened) change.

EORTC, European Organisation for Research and Treatment of Cancer; EOT, end of treatment; QLQ-C30, Quality of Life Questionnaire-Core 30; SD, standard deviation.

**Figure 2.** Mean change from baseline* in EORTC H&N35 subscale† scores over time
Mean baseline scores ± SD were 11.34 ± 18.41, 17.14 ± 37.96, and 5.25 ± 14.13 for trouble with social contact, weight loss, and head and neck pain subscales, respectively.

† Higher scores on the trouble with social contact subscale indicated positive (improved) change, while higher scores in weight loss and head and neck pain subscales indicated negative (worsened) change.

EORTC, European Organisation for Research and Treatment of Cancer; EOT, end of treatment; H&N35, Head and Neck Cancer Module 35; SD, standard deviation.

Treatment with sonidegib 200 mg daily appeared to maintain or improve QoL from baseline in most patients through 73 weeks. Observed worsening in weight loss scores may be expected due to dysgeusia. As EOT values were recorded at different timepoints, these scores often varied from the general trends, especially for EORTC QLQ-C30 subscales. Countertrends at EOT may also have resulted from decreased drug exposure from treatment holidays due to adverse events in the period leading to discontinuation. Our findings suggest that patients may have perceived that QoL benefits in most analyzed subscales outweighed occurring adverse effects of treatment. Maintenance or improvement of QoL in patients with aBCC—a difficult-to-
treat population—provides additional support for use of sonidegib as a viable treatment for these patients.
Abbreviations

aBCC, advanced basal cell carcinoma

BCC, basal cell carcinoma

BOLT, Basal Cell Carcinoma Outcomes with LDE225 Treatment

EORTC, European Organisation for Research and Treatment of Cancer

EOT, end of treatment

H&N35, Head and Neck Cancer Module 35

laBCC, locally advanced basal cell carcinoma

mBCC, metastatic basal cell carcinoma

QLQ-C30, Quality of Life Questionnaire-Core 30

QoL, quality of life

SD, standard deviation
References


