Sonidegib improved quality of life in patients with advanced basal cell carcinoma: Results from the phase 2 Basal cell carcinoma outcomes with LDE225 treatment trial through 73 weeks

To the Editor: 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 (Switzerland and Australia) and laBCC (United States and European Union).[3,4] Limited data exist regarding quality of life (QoL) in patients with advanced BCC.[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.

Basal Cell Carcinoma Outcomes with LDE225 Treatment 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. QLQ-C30 and H&N35 subscales most applicable to patients with advanced BCC 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 (Figs 1 and 2; Supplementary Table I and II, available via Mendeley at https://doi.org/10.17632/mm3xxgy6rm.1).

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.[5] As end-of-treatment values were recorded at different timepoints, these scores often varied from the general trends, especially for European Organisation for Research and Treatment of Cancer QLQ-C30 subscales. Countertrends at end of treatment 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 occurrent adverse effects of treatment. Maintenance or improvement of QoL in patients with advanced BCC—a difficult-to-treat population—provides additional support for use of sonidegib as a viable treatment for these patients.

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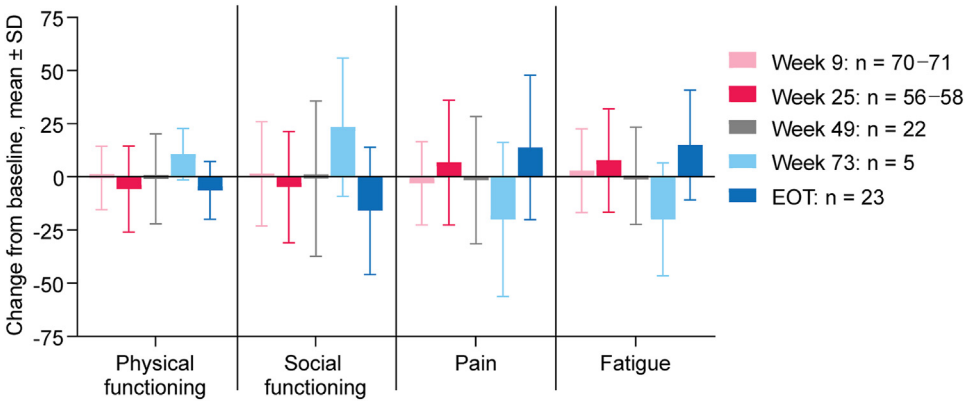

Fig 1. Mean change from baseline* in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 subscale† scores over time. *The mean baseline scores ± SD were 81.26 ± 22.39, 88.51 ± 18.49, 18.24 ± 24.23, and 21.70 ± 20.36 for physical functioning, social functioning, 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. *EOT*, End of treatment; *SD*, standard deviation.

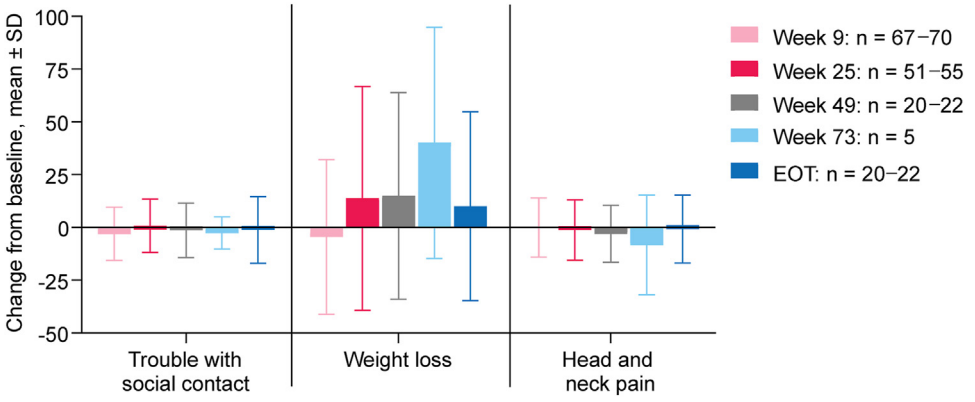

Fig 2. Mean change from baseline* in European Organisation for Research and Treatment of Cancer Head and Neck Cancer Module 35 subscale† scores over time. *The mean baseline scores ± SD were 11.34 ± 18.41, 17.14 ± 37.96, and 5.25 ± 14.13 for trouble with social contact, weight loss, and head and neck 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. *EOT*, End of treatment; *SD*, standard deviation.

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Patient consent form statement: All patient consent forms are on file.

Key words: advanced basal cell carcinoma; basal cell carcinoma; Hedgehog pathway inhibitor; metastatic basal cell carcinoma; quality of life; skin cancer; sonidegib.

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Conflicts of interest

Migden has participated on advisory boards and received honoraria from Genentech; Novartis; Sun Pharmaceutical Industries, Inc; and Regeneron. Loquai acted as a speaker for, participated in an advisory board for, and received honoraria from Bristol-Myers Squibb, Roche, Novartis, and Merck Sharp & Dohme. Robert has received consulting fees from Amgen, Array BioPharma, Bristol-Myers Squibb, Merck, Merck-Serono, Novartis, Pierre-Fabre, and Roche. Baurain reports that his institution has received fees for advisory boards from Bristol-Myer Squibb, Novartis, Pierre-Fabre, Sun Pharmaceutical, Sanofi-Regeneron, Amgen, Merck-Serono, and Merck Sharp & Dohme. Squittieri is an employee of Sun Pharmaceutical Industries, Inc. Arntz and Dierlamm are employees of Sun Pharmaceutical Industries, (Europe) B.V. Dréno 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.

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