Clinical, Cosmetic and Investigational Dermatology

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CASE REPORT

A Sonidegib Experience in the Treatment of Basal Cell Carcinoma with Systemic Lupus Erythematosus: A Case Report

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Abstract: Basal Cell Carcinoma (BCC), a prevalent skin cancer originating from keratinocytes, is mainly caused by the malfunctioning of the Hedgehog (Hh) signaling pathway. Surgical removal stands as the primary treatment, while non-invasive remedies encompass treatments like topical drug therapy, photodynamic therapy, radiotherapy, and molecular biologics, among others. For patients with locally advanced or metastatic basal cell carcinoma, agents targeting the Hedgehog signaling pathway, like sonidegib, have received approval, especially in cases where the lesion is inoperable or unsuitable for radiotherapy. Lupus erythematosus (LE), an autoimmune disorder, may include skin symptoms (such as discoid lupus erythematosus, DLE) and various systemic forms. Presently, there's a lack of documented clinical use of sonidegib in BCC patients alongside LE, particularly due to its unclear immunomodulatory impact on existing autoimmune diseases. In this report, we present a case involving a BCC patient and systemic lupus erythematosus (SLE), who received sonidegib treatment yielding positive results without simultaneously triggering lupus erythematosus activity.
Keywords: basal cell carcinoma, systemic lupus erythematosus, sonidegib, targeted therapy, immune

Introduction

Basal cell carcinoma ranks as the predominant skin cancer, making up 80% of non-melanoma skin cancers (NMSC), with its worldwide occurrence rate showing a consistent yearly rise of about 10%.[1,2] The development of BCC is mainly ascribed to exposure to ultraviolet light, genetic predisposition, and the unregulated triggering of the Hedgehog signaling pathway.[3,4] Most BCC cases are operable and treatable. However, cases of locally advanced BCC (laBCC) or metastatic BCC continue to depend on specific systemic treatments,[5,6] such as the US-approved Hedgehog pathway inhibitor (HHI) sonidegib. In 2015, the Food and Drug Administration (FDA) was responsible for the treatment of laBCC patients who could not undergo curative resection or radiotherapy.[7] The Hedgehog (Hh) pathway is critical for basal cell proliferation and frequently dysregulated in basal cell carcinoma (BCC). This evolutionarily conserved pathway supports embryonic development and maintains adult skin homeostasis, hair follicle regeneration, and stem cell self-renewal. Physiologically, PTCH1 negatively regulates SMO, a G protein-coupled receptor. In BCC, tumorigenesis primarily arises from ligand-independent PTCH1 mutations (85–90%) or SMO mutations (10%), leading to constitutive activation of the Hh signaling pathway.[6,8,9] By specifically inhibiting the Smoothened (SMO) receptor, a crucial element in the Hedgehog signaling pathway, sonidegib hinders the advancement of basal cell carcinoma.[9] Sonidegib, through its targeted interaction with SMO, reduces the overactivation of the Hh pathway, thereby inhibiting the growth and spread of tumor cells.[10–13] The effectiveness of sonidegib in treating laBCC is largely attributed to this specific mechanism.

Received: 2 August 2025
Accepted: 30 October 2025
Published: 21 November 2025

Nonetheless, individuals suffering from simultaneous systemic lupus erythematosus (SLE) or chronic cutaneous lupus erythematosus (CCLE) encounter distinct treatment hurdles: chronic inflammation and immune imbalance linked to lupus can intensify BCC aggression,[14–16] while conventional immunosuppressants (eg, the use of corticosteroids and anti-malarials could jeopardize anti-cancer therapies,[17] while localized treatments like surgery and radiotherapy might worsen the condition in areas affected by lupus lesions[18,19]).

Present studies on the application of HHI in autoimmune disease patients are still scarcely recorded. Sonidegib, being a second-generation HHI, achieves cancer-fighting properties by specifically attaching to SMO, yet its possible immunomodulatory impacts and safety/efficacy characteristics are still unclear. Here, we initially present a case of a patient suffering from locally advanced facial BCC, alongside persistent SLE, who attained Complete Response (CR) and experienced no SLE disease activity via sonidegib treatment. The case offers a framework grounded in evidence for the meticulous handling of intricate conditions.

Case Presentation

A 65-year-old woman came to the clinic in August 2024, reporting a 36-month struggle with ongoing non-healing nasal skin ulcers. She has been battling lupus erythematosus for over two decades and has been on multiple medications for an extended period to manage the disease's advancement, including Methylprednisolone Tablets 4mg/day, Calcitriol Soft Capsules 0.25μg/day, and Hydroxychloroquine Sulfate Tablets 0.1g/day. In September 2023, the patient's nasal skin experienced a relapse, which was eventually treated medically. The lesion was histopathologically confirmed as basal cell carcinoma (BCC) in June 2024 (Figure 1). Owing to the prolonged use of immunosuppressive drugs, potential challenges in wound healing post-surgery, and significant effects on her looks, the patient declined surgical intervention. Following a thorough evaluation, the patient was given 200 mg/day of oral sonidegib (ODOMZO)®, and the patient's blood and biochemical indicators were tracked at the start, one month, three months, and six months to document any potential clinical side effects. Before initiation of the targeted therapy, the patient's clinical symptoms of SLE and relevant disease activity indices were all stable. The patient adhered well to the treatment regimen, consistently consuming 200mg/day sonidegib, 4mg/day Methylprednisolone Tablets, 0.25μg/day Calcitriol Soft Capsules, and 0.1g/day Hydroxychloroquine Sulfate Tablets. The subsequent check-up revealed that the patient's nasal sores had been progressively abrading and diminishing in size since starting the medication, with the images indicating that recovery was essentially realized after a 6-month treatment period (Figure 2). Throughout the treatment, the patient's levels of hemoglobin, lymphocyte count, creatine kinase, creatinine, glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and amylase largely stayed within normal limits, exhibiting no notable variations (Table 1). Since the administration of the medication, the patient has been free from negative side effects like muscle spasms, taste disturbances, or diminished appetite, and no reoccurrences of lupus erythematosus have been noted during the therapy. During the follow-up period, as the patient self-reported subjective improvement in cutaneous lesions with no other significant discomfort, she declined dermoscopic examination and comprehensive assessment of SLE activity markers (including complement levels and anti-dsDNA antibody titers), thereby precluding the acquisition of these diagnostic parameters. As a result, our analysis was confined to lupus-associated biomarkers derived from the patient's most recent routine blood tests, all of which remained within normal reference ranges (Table 2).

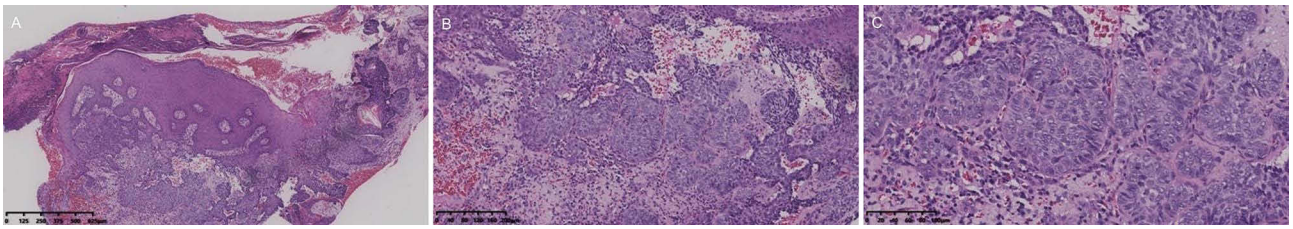

Figure 1 Pathological section of nasal skin ulcer. (**A**) Low-power view showing tumor cell nests within the dermis connected to the epidermis (H&E; original magnification ×40). (**B**) Medium-power view highlighting the nested growth pattern of tumor cells (H&E; original magnification ×100). (**C**) High-power view demonstrating peripheral palisading of tumor cells with clear borders and mucinous degeneration in the surrounding stroma (H&E; original magnification ×200).

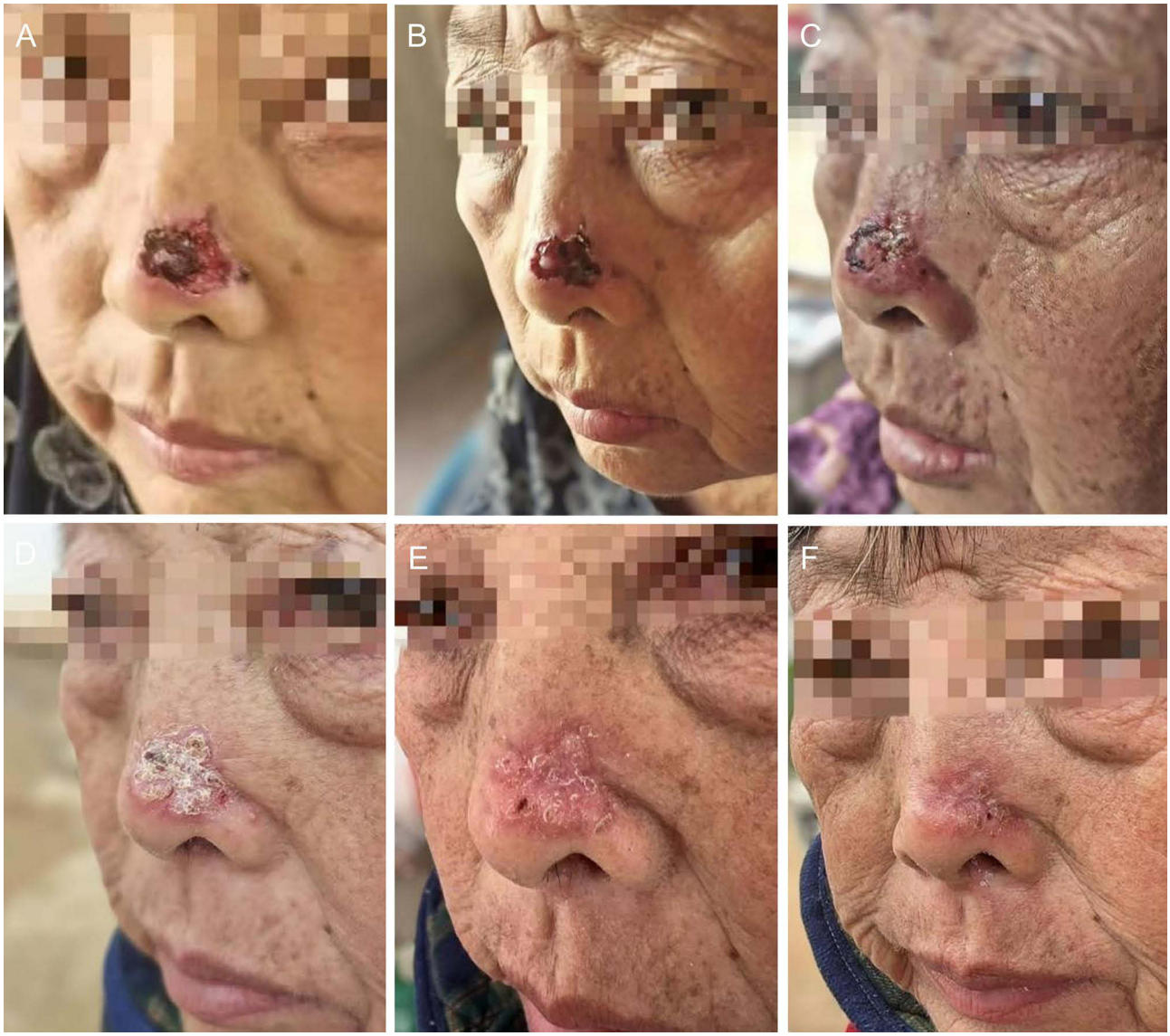

Figure 2 Photographs of basal cell carcinoma in a patient with lupus erythematosus who achieved complete clearance following treatment with sonidegib. (**A**) Before treatment, a coin-sized skin lesion is visible on the left side of the nose, with part of it covered by a thick brown crust and the other part showing a shallow ulceration with a red appearance. (**B**) 1 month of treatment, the thick crust at the lesion site mentioned above has fallen off, revealing a fresh red base surface with scattered blood scabs, and white scales can be seen around the edge. (**C**) 2 months of treatment, there is an erythematous patch approximating the size of the original lesion, exhibiting a central brown crust and yellow-white scales, and no evidence of ulceration. (**D**) 4 months of treatment, the erythematous patch remains unchanged in size, overlaid with diffuse yellow-white scales. (**E**) 5 months of treatment, the erythematous patch remains unchanged in size, with scattered thin yellow-white scales. (**F**) 6 months of treatment, the erythematous patch has slightly decreased in size compared to prior observations, with scattered sparse round yellow crusts.

Discussion

Currently, two Hedgehog pathway inhibitors (HHIs), namely sonidegib and vismodegib, have received approval for the systemic treatment of laBCC and metastatic BCC. To date, no conclusive evidence has emerged to demonstrate significant differences between these two drugs in terms of their therapeutic efficacy and drug resistance profiles.[20,21] Furthermore, only sonidegib is currently accessible in the Chinese market. This instance marks the inaugural recorded use of sonidegib, which has proven effective in treating both conditions: locally advanced basal cell carcinoma (laBCC) and SLE. The result not only introduces an innovative approach to treating intricate multimorbidities but also reveals the possible immunomodulatory impact of Hedgehog pathway inhibitors (HHIs), possibly expanding their use in clinical settings.

By inhibiting the Smoothened (SMO) receptor, HHIs curtail the continuous activation of the Hedgehog pathway and additionally hinder BCC's growth and spread. Remarkably, the patient attained a full response (CR) while keeping SLE

Table 1 Lab Results Pertaining to Sonidegib Pre and Post-Treatment

	1st Month	2nd Month	3rd Month	Normal Range
Hemoglobin (Hb)	136g/L	134g/L	135g/L	110-150 g/L
Lymphocyte count	0.91×10^9/L	1.42×10^9/L	0.94×10^9/L	$0.8–4.0\times10^9$/L
Alanine aminotransferase (ALT)	23U/L	25U/L	26U/L	2-40 U/L
Aspartate transaminase (AST)	30U/L	33U/L	31U/L	2-40 U/L
Glucose	4.92mmol/L	5mmol/L	4.9mmol/L	3.9–6.1 mmol/L
Creatine kinase (CK)	161U/L	178U/L	170U/L	40-200 U/L
Creatinine (Cr)	59.7μmol/L	63μmol/L	59μmol/L	44-97 μmol/L

Table 2 Certain SLE Disease Activity Indicators After a 6-Month Therapy

Items	Test Result	Frame of Reference
Hemoglobin (Hb)	135	115-150g/L
Platelet (Plt)	152×10^9	$(125–350)\times10^9$/L
C-reactive protein (CRP)	<10	0-10mg/L
Erythrocyte Sedimentation Rate (ESR)	36	0-15mm/H

activity regulated, indicating sonidegib's possible immunomodulatory impact on immune cells from the tumor microenvironment (TME), indirectly influencing autoimmune reactions.[2,3] Animal studies demonstrate that HHIs reduce the levels of pro-inflammatory cytokines (eg, IL-6, TNF-α),[22–24] which may explain the sustained remission of SLE in this patient. In contrast to conventional immunosuppressants such as glucocorticoids, sonidegib's treatment approach avoids the need for a wide range of immune inhibitors,[21] thus reducing the likelihood of secondary infections and the unexpected advancement of cancer.

Earlier Basal Cell Carcinoma Outcomes With Sonidegib (LDE225) Treatment (BOLT) studies showed that sonidegib therapy for advanced BCC achieved a 58% objective response rate,[25] yet deliberately omitted patients with autoimmune coexisting conditions. The case we present shows a full response (CR) in line with BOLT effectiveness standards, keeping lupus in a dormant state without significant adverse effects (AE) from the treatment, thereby questioning the common belief that targeted treatments would increase risk in populations with immune dysregulation.[26–28] Furthermore, the patients with SLE had significantly increased associations with non-melanoma skin cancer (NMSC),[29] owing to prolonged use of immunosuppressants and persistent inflammation mediated by IFN-α. Targeted treatment with sonidegib presents a more secure option for such populations.

Typical adverse effects (AE) associated with sonidegib include muscle spasms (71.2%), alopecia (66.3%), and dysgeusia (55.8%), which did not happen in this patient.[30,31] Fascinatingly, this patient showed no signs of immune-related adverse effects (irAEs), like interstitial pneumonitis or colitis, possibly due to sonidegib's unique molecular action mechanism, distinct from immune checkpoint inhibitors (ICIs). However, it is essential to remain vigilant for potential musculoskeletal toxicity and developing tumor resistance during prolonged HHI therapy. Therefore, regular monitoring should include creatine kinase (CK) level testing and radiological assessments.

While this instance presents initial evidence of sonidegib's therapeutic efficacy in the management of BCC in a patient with connective tissue disease undergoing chronic immunosuppressive therapy, its confinement to a single-center observational setting constrains the final judgment. The specific pharmacological effects of HHI on lupus-related immune disorders, especially IFN-I signaling, are yet to be clarified. Upcoming studies ought to utilize single-cell sequencing (sc-seq) and Multiplex Immunofluorescence (mIF) for clarifying the dynamic interplay between tumors and

the immune microenvironment (TIME). In cases where patients exhibit active systemic lupus erythematosus or significant organ complications, a comprehensive assessment of sonidegib treatment's safety is essential.

Conclusion

In this single case, sonidegib demonstrated promising efficacy and manageable safety in a patient with BCC who was ineligible for surgery due to SLE and concurrent long-term oral immunosuppressive therapy. However, these observations are preliminary and cannot be generalized to broader populations. Further studies involving larger cohorts are warranted to confirm the therapeutic potential, safety, and generalizability of sonidegib in similar high-risk patient groups.

Ethics Statement

Written informed consent has been provided by the patient to have the case details and any accompanying images published. Publication of details of the case does not require the agency's approval.

Consent Statement

The patient had given written informed consent for the publication of her clinical details.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was supported by Jiangxi Provincial Natural Science Foundation (No. 20242BAB26145), the National Natural Science Foundation of China (No. 81860484).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Agbai ON, Buster K, Sanchez M, et al. Skin cancer and photoprotection in people of color: a review and recommendations for physicians and the public. *J Am Acad Dermatol*. 2014;70(4):748–762. doi:10.1016/j.jaad.2013.11.038
2. Garcovich S, Colloca G, Sollena P, et al. Skin cancer epidemics in the elderly as an emerging issue in geriatric oncology. *Aging Dis*. 2017;8(5):643–661. doi:10.14336/ad.2017.0503
3. Chmiel P, Kłosińska M, Forma A, Pelc Z, Gęca K, Skórzewska M. Novel approaches in non-melanoma skin cancers-A focus on hedgehog pathway in basal cell carcinoma (BCC). *Cells*. 2022;11(20):3210. doi:10.3390/cells11203210
4. Onishi H, Katano M. Hedgehog signaling pathway as a therapeutic target in various types of cancer. *Cancer Sci*. 2011;102(10):1756–1760. doi:10.1111/j.1349-7006.2011.02010.x
5. Svoboda SA, Johnson NM, Phillips MA. Systemic targeted treatments for basal cell carcinoma. *Cutis*. 2022;109(6):E25–e31. doi:10.12788/cutis.0560
6. Leavitt E, Lask G, Martin S. Sonic hedgehog pathway inhibition in the treatment of advanced basal cell carcinoma. *Curr Treat Options Oncol*. 2019;20(11):84. doi:10.1007/s11864-019-0683-9
7. Casey D, Demko S, Shord S, et al. FDA approval summary: sonidegib for locally advanced basal cell carcinoma. *Clin Cancer Res*. 2017;23(10):2377–2381. doi:10.1158/1078-0432.Ccr-16-2051
8. Gambini D, Passoni E, Nazzaro G, et al. Basal cell carcinoma and hedgehog pathway inhibitors: focus on immune response. *Front Med*. 2022;9:893063. doi:10.3389/fmed.2022.893063
9. Basset-Seguin N, Sharpe HJ, de Sauvage FJ. Efficacy of hedgehog pathway inhibitors in basal cell carcinoma. *Mol Cancer Ther*. 2015;14(3):633–641. doi:10.1158/1535-7163.Mct-14-0703
10. Barakat MT, Humke EW, Scott MP. Learning from Jekyll to control Hyde: hedgehog signaling in development and cancer. *Trends Mol Med*. 2010;16(8):337–348. doi:10.1016/j.molmed.2010.05.003
11. Wahid M, Jawed A, Mandal RK, et al. Vismodegib, itraconazole and sonidegib as hedgehog pathway inhibitors and their relative competencies in the treatment of basal cell carcinomas. *Crit Rev Oncol Hematol*. 2016;98:235–241. doi:10.1016/j.critrevonc.2015.11.006
12. Jain S, Song R, Xie J. Sonidegib: mechanism of action, pharmacology, and clinical utility for advanced basal cell carcinomas. *Onco Targets Ther*. 2017;10:1645–1653. doi:10.2147/ott.S130910

13. Villani A, Fabbrocini G, Costa C, Scalvenzi M. Sonidegib: safety and efficacy in treatment of advanced basal cell carcinoma. *Dermatol Ther*. 2020;10(3):401–412. doi:10.1007/s13555-020-00378-8
14. Wunderlich K, Suppa M, Gandini S, Lipski J, White JM, Del Marmol V. Risk factors and innovations in risk assessment for melanoma, basal cell carcinoma, and squamous cell carcinoma. *Cancers*. 2024;16(5):1016. doi:10.3390/cancers16051016
15. Wen Y, Zhu Y, Zhang C, et al. Chronic inflammation, cancer development and immunotherapy. *Front Pharmacol*. 2022;13:1040163. doi:10.3389/fphar.2022.1040163
16. Lefrançois P, Xie P, Gunn S, et al. In silico analyses of the tumor microenvironment highlight tumoral inflammation, a Th2 cytokine shift and a mesenchymal stem cell-like phenotype in advanced in basal cell carcinomas. *J Cell Commun Signal*. 2020;14(2):245–254. doi:10.1007/s12079-020-00563-6
17. Bruera S, Suarez-Almazor ME. The effects of glucocorticoids and immunosuppressants on cancer outcomes in checkpoint inhibitor therapy. *Front Oncol*. 2022;12:928390. doi:10.3389/fonc.2022.928390
18. Dąbrowska AM, Słotwiński R. The immune response to surgery and infection. *Cent Eur J Immunol*. 2014;39(4):532–537. doi:10.5114/ceji.2014.47741
19. Lachmann G, von Haefen C, Kurth J, Yuerek F, Spies C. Innate immunity recovers earlier than acquired immunity during severe postoperative immunosuppression. *Int J Med Sci*. 2018;15(1):1–9. doi:10.7150/ijms.21433
20. Migden MR, Chang ALS, Dirix L, Stratigos AJ, Lear JT. Emerging trends in the treatment of advanced basal cell carcinoma. *Cancer Treat Rev*. 2018;64:1–10. doi:10.1016/j.ctrv.2017.12.009
21. Dummer R, Ascierto PA, Basset-Seguin N, et al. Sonidegib and vismodegib in the treatment of patients with locally advanced basal cell carcinoma: a joint expert opinion. *J European Acad Dermatol Venereol*. 2020;34(9):1944–1956. doi:10.1111/jdv.16230
22. Kangwan N, Kim YJ, Han YM, et al. Sonic hedgehog inhibitors prevent colitis-associated cancer via orchestrated mechanisms of IL-6/gp130 inhibition, 15-PGDH induction, Bcl-2 abrogation, and tumorsphere inhibition. *Oncotarget*. 2016;7(7):7667–7682. doi:10.18632/oncotarget.6765
23. Chen X, Jin Y, Hou X, Liu F, Wang Y. Sonic hedgehog signaling: evidence for its protective role in endotoxin induced acute lung injury in mouse model. *PLoS One*. 2015;10(11):e0140886. doi:10.1371/journal.pone.0140886
24. Kangwan N, Kim YJ, Han YM, Jeong M, Park JM, Hahm KB. Concerted actions of ameliorated colitis, aberrant crypt foci inhibition and 15-hydroxyprostaglandin dehydrogenase induction by sonic hedgehog inhibitor led to prevention of colitis-associated cancer. *Int J Cancer*. 2016;138(6):1482–1493. doi:10.1002/ijc.29892
25. Migden MR, Guminski A, Gutzmer R, et al. Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): a multicentre, randomised, double-blind Phase 2 trial. *Lancet Oncol*. 2015;16(6):716–728. doi:10.1016/s1470-2045(15)70100-2
26. Björnådal L, Löfström B, Yin L, Lundberg IE, Ekbom A. Increased cancer incidence in a Swedish cohort of patients with systemic lupus erythematosus. *Scand J Rheumatol*. 2002;31(2):66–71. doi:10.1080/03009740252937568
27. Chen YJ, Chang YT, Wang CB, Wu CY. Malignancy in systemic lupus erythematosus: a nationwide cohort study in Taiwan. *Am J Med*. 2010;123(12):1150.e1151–1156. doi:10.1016/j.amjmed.2010.08.006
28. Dreyer L, Faurschou M, Mogensen M, Jacobsen S. High incidence of potentially virus-induced malignancies in systemic lupus erythematosus: a long-term followup study in a Danish cohort. *Arthritis Rheum*. 2011;63(10):3032–3037. doi:10.1002/art.30483
29. Tseng HW, Huang WC, Lu LY. The influence of immunosuppressants on non-melanoma skin cancer among patients with systemic lupus erythematosus and primary Sjögren's syndrome: a nationwide retrospective case-control study in Taiwan. *Clin Experimental Rheumatol*. 2019;37(6):946–952. doi:10.3333/cer.2019.37.6.946
30. Wahid M, Jawed A, Dar SA, Mandal RK, Haque S. Differential pharmacology and clinical utility of sonidegib in advanced basal cell carcinoma. *Onco Targets Ther*. 2017;10:515–520. doi:10.2147/ott.S97713
31. Basset-Seguin N, Hauschild A, Grob JJ, et al. Vismodegib in patients with advanced basal cell carcinoma (STEVIE): a pre-planned interim analysis of an international, open-label trial. *Lancet Oncol*. 2015;16(6):729–736. doi:10.1016/s1470-2045(15)70198-1