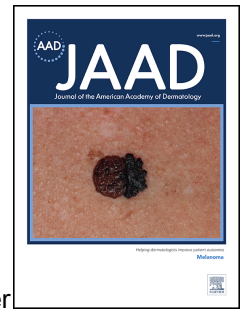

Clinical Practice Guidelines for the Management of Basal Cell Carcinoma in Gorlin Syndrome

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Abstract

Background: Gorlin syndrome (GS) is a rare genetic disorder characterized by a predisposition to developing numerous basal cell carcinomas (BCCs) throughout life. The absence of specific clinical guidelines for managing BCCs in GS has resulted in fragmented care and inconsistent treatment approaches.

Objective: To develop evidence-based guidelines for managing BCCs in GS, addressing both clinical and psychosocial challenges.

Methods: A multidisciplinary panel employed a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, integrating systematic reviews, expert surveys, patient interviews, and Delphi consensus rounds to formulate recommendations.

Results: The final guidelines include 47 recommendations spanning topical therapies, systemic treatments, surgical interventions, and multimodal strategies. Additional recommendations emphasize shared decision-making, comprehensive monitoring, and psychosocial support to address the chronic nature of BCCs in GS. Specific therapies, including hedgehog inhibitors and field treatments, are recommended to reduce surgical fatigue and enhance quality of life.

Limitations: Given the scarcity of GS-specific data, expert consensus informed several recommendations, highlighting the need for ongoing research to strengthen the evidence base.

Conclusion: These guidelines provide a structured framework for improving BCC management in GS, thereby enhancing clinical outcomes and patient quality of life. This process serves as a model for creating patient-centered guidelines in rare conditions with limited evidence.

Capsule Summary

- Comprehensive, evidence-based guidelines for managing basal cell carcinomas in Gorlin Syndrome are lacking.
- Our recommendations provide dermatologists with a practical framework for selecting appropriate treatment options, reducing surgical burden, improving quality of life, and integrating psychosocial support for long-term management of this unique patient population.

Introduction

Gorlin syndrome (GS), also known as nevoid basal cell carcinoma syndrome, is an autosomal dominant genetic disorder characterized by the development of numerous basal cell carcinomas (BCCs) over a patient's lifetime. The disorder results from mutations in the PTCH1 or SUFU genes, affecting the hedgehog signaling pathway, which plays a crucial role in embryonic development and tumor suppression.[1] Individuals with GS experience a lifelong burden of BCCs, along with other manifestations such as odontogenic keratocysts, skeletal anomalies, and increased risk of other tumors.[2]

Despite the disease burden of multiple disfiguring and potentially function-impairing BCCs, there are no standardized clinical guidelines specifically addressing the management of BCCs in GS patients.[3] Existing recommendations for sporadic BCCs often do not adequately address the

challenges faced by GS patients (Supplementary Figure I), selection of appropriate treatments, surgical fatigue, extensive disease burden, psychosocial impact, curative versus palliative intent, and the need for lifelong multidisciplinary care.[4]

To facilitate the delivery of evidence-based care prioritizing patient quality of life and long-term outcomes, clinical practice guidelines tailored to the needs of GS patients, including clinical and psychological aspects of care, were developed.

Methods

The guideline development process followed a modified GRADE methodology and involved multiple stages, including the development of an expert panel, the creation of initial PICO (Population, Intervention, Comparison, Outcome) questions, systematic literature reviews, expert evidence surveys, structured patient interviews, Delphi consensus rounds, and a final consensus meeting.[5]

Expert Panel Development and Composition

The steering committee, consisting of clinicians and researchers with expertise in GS, identified as potential panelists across various specialties, ensuring at least 51% had no financial conflicts of interest.[6] Panelists were selected based on their clinical experience, research contributions, and engagement in patient care. Invitations were extended to specialists in dermatology, Mohs surgery, pediatric dermatology, oncodermatology, dermatopathology, pediatrics, adult and pediatric genetics, adult and pediatric oncology, psychiatry, psychology, cancer biology, cell biology, radiation oncology, and oral and maxillofacial surgery. Patients with GS and family members also served on the panel, with some from the Gorlin Syndrome Alliance (GSA), a patient advocacy group (Supplementary Table I).

Creation of Initial PICO Questions

The guidelines committee formulated a set of PICO questions to ensure that the recommendations would address the most relevant and pressing clinical issues in the management of BCC in GS. These questions were designed to cover a wide range of topics, including prevention strategies, treatment modalities, monitoring protocols, psychosocial support, and other key areas. The PICO framework provided a structured approach to evaluating the available evidence and identifying gaps in knowledge that required further exploration.

Systematic Review

A comprehensive review of the literature was conducted to identify evidence on BCC management strategies in GS patients. The review included randomized controlled trials, cohort studies, case-control studies, and case series involving 10 or more patients. The search strategy (Supplementary Table II) and screening process were supported by research librarians from the

University of Illinois Chicago to ensure comprehensiveness and accuracy. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist was used to guide the review process (Supplementary Figure II).[7] To manage the screening and data extraction process, the Covidence platform was used.[8]

Expert Evidence Surveys

Given the limited availability of high-quality evidence specific to GS, the panel designed and distributed expert evidence surveys to gather insights from clinicians with experience treating GS patients (Supplementary Table III).[9] These surveys focused on understanding treatment preferences, perceived effectiveness of various modalities, and approaches to patient management. Both qualitative and quantitative data were obtained.

Patient Interviews

Structured interviews were conducted with individuals affected by GS to ensure that patient perspectives were integrated into the guideline development process (Supplementary Table IV).[9] The interviews captured patient preferences and experiences with various treatments.[10]

Provisional Recommendation Development

Initial provisional recommendations were developed by subcommittees assigned to various PICO questions.[11] These subcommittees considered their own clinical experience in addition to data from the systematic review, expert evidence surveys, and qualitative one-on-one patient interviews.

Delphi Consensus Process

The draft recommendations were refined through a structured two-round Delphi process.[12] In the first round, the entire panel reviewed each draft recommendation and rated their agreement using a 9-point Likert scale. Recommendations that were close to the consensus cutoff were revised and resubmitted for a second round of voting. Recommendations exceeding the consensus threshold were retained, while those below were removed.

Following the Delphi rounds, a final consensus meeting was held to review draft recommendations and address areas of disagreement. Based on a high consensus threshold (>90%), adjustments were made to improve the clarity and applicability of the recommendations. This meeting also provided an opportunity to identify any remaining evidence gaps and prioritize future research directions (Supplementary Figure III).

Results

The multidisciplinary panel ultimately included over 130 members, ensuring a broad range of expertise necessary for addressing the complexities of managing BCC in GS (Supplementary

Table I). Subcommittees were formed to address specific PICO questions, with experts assigned based on their specialty. Additionally, 87% of the panel had no financial conflicts of interest. The panel subcommittees generated 60 provisional recommendations, of which 47 were refined and adopted following two Delphi rounds and a consensus meeting. The final recommendations addressed treatment modalities, prevention strategies, psychosocial support, patient education, and long-term monitoring.

The complete recommendations, detailed in Tables I–V, cover a wide range of topics, including topical and systemic therapies, multimodal treatments, and surgical, photodynamic, laser, destructive, and radiation therapies. Additionally, they address monitoring, prevention, imaging, and multidisciplinary care; mental health, genetics, clinical trials, and special considerations; as well as disease severity, lesion prioritization, psychosocial impact, and financial burden. Major findings are summarized below.

Topical Treatments

Topical therapies are key to managing low-risk BCCs, addressing field cancerization, and to minimize surgical fatigue. The guidelines recommend topical 5-fluorouracil and imiquimod as primary topical therapies. Topical therapies can also be used to clear positive superficial surgical margins in low-risk tumors.

Systemic Therapies

Hedgehog pathway inhibitors (HHIs) are recommended for patients with multiple low-risk tumors or high-risk disease where surgery would cause functional impairment or disfigurement. Intermittent dosing and treatment holidays improve quality of life by reducing side effects. Patients with SUFU mutations should not receive the current generation of HHIs. PD-1 inhibitors are only considered in high-risk disease cases when other systemic therapies have been unsuccessful.

Surgical Approaches

Surgery remains essential for high-risk BCCs in GS patients (Supplementary Figure IV). When surgery is selected, it should aim to minimize scarring, functional impairment and surgical fatigue. For low-risk tumors, achieving negative deep histologic margins may suffice to avoid unnecessary disfigurement. Conservative reconstruction is preferred given the likelihood of future tumors and to avoid transposing tumors into the defect.

Photodynamic and Laser Therapies

Photodynamic therapy (PDT) may be recommended for low-risk BCCs in patients who tolerate it. PDT can be used for individual lesions or field therapy. Laser treatments, such as vascular or ablative lasers, are discussed as adjunctive but not first-line therapies.

Prevention and Monitoring

Prevention strategies emphasize strict sun protection, including sun protection and behavioral changes. Routine skin examinations, dermoscopy, and high-resolution photography are recommended for early tumor identification. Patient education is crucial, with self-examinations and active participation in care.

Multimodal Approaches

A multimodal approach is critical for managing GS-related BCCs. Integrating lesion-specific therapies with field treatments and shared decision-making is recommended. Multidisciplinary care, involving dermatologists, geneticists, oncologists, and mental health professionals, addresses the comprehensive needs of GS patients.

Psychosocial Support and Patient Education

As with sporadic BCC, psychosocial support is essential for improving patient outcomes. Mental health support should be incorporated into care plans. Recommendations include access to counseling services, support networks, and patient advocacy groups such as the GSA.

Discussion

The development of guidelines for managing BCCs in GS posed unique challenges due to the rarity of the condition and the consequent limited availability of high-quality evidence. Guidelines for GS require consideration of the chronic and recurring nature of the disease, as well as the psychosocial impact on patients.

Shared Decision-Making

Shared decision-making emerged as a central theme throughout the guideline development process. The chronic nature of GS necessitates a personalized approach to care. Patients consistently expressed the need to balance aggressive treatments with quality-of-life considerations, particularly when managing multiple lesions over a lifetime. The panel recognized that empowering patients to participate in treatment decisions fosters better adherence and improves overall satisfaction with care. Still, achieving true shared decision-making can be challenging, especially when patients have differing levels of health literacy. The guidelines emphasize clear communication and the use of decision aids to help patients understand their options and the potential risks and benefits of each approach.

There was significant variation in how patients perceive risk and benefit. Some patients preferred more aggressive surgical treatments to achieve long-term control, while others prioritized minimizing the impact on their lives with less invasive surgical or non-surgical methods. This underscores the importance of shared decision-making as a dynamic process that must be tailored to individual patient values as a dynamic that must be tailored to individual patient preferences. In cases in which less aggressive approaches are likely to result in patient harm, it is the clinician’s responsibility to communicate the relevant risks and benefits so that patient and clinician can jointly reach a prudent decision.

Surgical Fatigue and Non-Invasive Alternatives

While surgery remains the mainstay of treatment for many patients given the balance of risks and benefits, concern about surgical fatigue was repeatedly raised by both patients and clinicians. GS patients often require numerous surgical procedures throughout their lives, leading to physical and psychological exhaustion. This observation influenced several recommendations, particularly those advocating for non-invasive treatments such as topical therapies and systemic medications. The panel debated the appropriate use of HHIs, with some members emphasizing their role in reducing surgical burden, while others cautioned about side effects that can be persistent and life-altering. Ultimately, the guidelines recommend HHIs for patients with a high tumor burden or when surgical interventions would result in significant disfigurement. Intermittent dosing and treatment holidays were recommended to improve tolerability.

Psychosocial Impacts and Mental Health Support

The psychosocial impact of living with GS and recurrent BCCs cannot be overstated.[13-17] Many patients reported experiencing anxiety, depression, and social isolation due to their visible lesions and scars and the frequency of medical appointments and interventions. The panel acknowledged that addressing these psychosocial impacts is essential for improving overall quality of life. The guidelines advocate for providing patients with access to counseling services, support groups, and patient advocacy organizations such as the GSA. The inclusion of psychosocial support recommendations underscores the importance of holistic, patient-centered care. Future research should focus on developing targeted interventions to support the psychological well-being of GS patients. Special training on managing GS patients may also need to be provided to caregivers.

Multidisciplinary Care and Coordination

A key takeaway from the guideline development process is the importance of multidisciplinary care in managing GS. In addition to receiving care from dermatologists, GS patients have non-dermatologic needs that may be addressed by other physicians and non-physicians including dentists, neurologists, oncologists, mental health professionals and others. The panel discussed the need for care coordinators or case managers to help streamline appointments and ensure that patients receive comprehensive care. While this recommendation is not included in guidelines since variability in healthcare systems may make it impractical in certain cases, it remains an important consideration for improving patient experiences.

The guidelines also emphasize the role of genetic counseling. Given the hereditary nature of GS, genetic counseling can help patients understand their risk of passing the condition to future generations and inform family planning decisions. The availability of genetic counseling services also varies widely, and this remains an area for future improvement.

Provisional Recommendations That Were Not Included in the Final Guidelines

Several recommendations were debated but ultimately were not included in the final guidelines due to insufficient evidence or lack of consensus. Notable examples include the use of telehealth for monitoring patients and oral nicotinamide as a chemopreventive agent.

Telehealth

There was considerable discussion regarding using telehealth and electronic medical records to monitor patients remotely and reduce the frequency of in-person visits. Proponents argued that telehealth could empower patients to monitor their own lesions and improve shared decision-making. Concerns were raised about the variability in patients' ability to accurately document and report changes in their lesions, leading to a decision to omit a specific recommendation on telehealth. Telehealth is promising, but the lack of protocols limits its use in GS patients.

Oral Nicotinamide

Although studies in non-Gorlin populations suggested a modest benefit of nicotinamide in reducing non-melanoma skin cancers, conflicting evidence and concerns about potential cardiotoxic effects led to its exclusion from the final recommendations.[18, 19] Some panel members viewed it as a low-risk intervention that was unlikely to be associated with adverse events, while others expressed reservations that it might provide a false sense of security without proven efficacy.

Genetic Testing and Emerging Therapies

PICO questions related to the role of routine genetic testing and emerging therapies, such as topical HHIs and mTOR inhibitors, did not lead to recommendations due to limited evidence.[20, 21] Although these therapeutic approaches are promising, they remain experimental and require further research. The panel agreed that patients should be informed of ongoing clinical trials in which they may be eligible to participate.

Limitations of the Guidelines

The guidelines acknowledge several limitations. There is limited high-quality evidence specific to GS. Many recommendations are based on expert consensus and evidence extrapolated from studies on sporadic BCCs. These guidelines are designed for the US healthcare system and may be adaptable to other similar healthcare systems but be less feasible in other less resourced systems. Patient preferences and values can vary significantly, underscoring the importance of tailoring treatments to individual needs. While the panel considered the needs of GS patients with only a small number of BCCs, none of the patient panelists had skin of color, which limits generalizability. Telehealth as a monitoring tool and regional specialist networks may help mitigate barriers to care.

Future Directions and Research Priorities

Despite growing clinical experience, significant evidence gaps remain in the management of BCC in GS. Key priorities include determining the optimal use, timing, and long-term safety of

hedgehog inhibitors (HHIs); evaluating preventative and field-directed therapies; and establishing surveillance strategies for pediatric and adolescent patients. Much of current practice relies on expert consensus, underscoring the need for prospective studies and randomized trials specific to this population.

Additional research may focus on standardizing surveillance protocols, developing GS-specific quality-of-life metrics, and understanding real-world barriers to care, including access to multidisciplinary expertise and insurance coverage. Consolidation and expansion of existing GS registries[22] could enhance data quality, support multicenter collaboration, and enable ongoing refinement of management strategies. Equally important is patient-centered qualitative research to better characterize the psychosocial burden of disease and the factors driving treatment preferences.

While cure remains an aspirational objective, the realistic current goals of cancer care in GS patients are control of the tumor burden and preservation of quality of life. These guidelines provide a framework for shared decision-making, multidisciplinary care, and evidence-informed, individualized treatment planning.

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Table I. Recommendations for Topical and Systemic Therapies and Multimodal Treatments

Rec 1: When treating BCC in GS, use of topical therapeutics including topical 5-FU and imiquimod should be considered when feasible as primary treatment for low-risk tumors, for field effect, and to minimize surgical fatigue. (◆, ●)
Rec 2: When treating BCC in GS, topical therapeutics including topical 5-FU and imiquimod may be considered to clear positive superficial surgical margins in low-risk tumors. (◆, ●)
Rec 3: Escharotics should not be used to treat BCC in patients with GS since they may result in unnecessary disfigurement and morbidity. (◆, ●)
Rec 4: When treating BCC in GS, systemic therapy may be considered for patients with multiple low-risk tumors; or high-risk disease with fewer BCC but those for which surgery may result in functional impairment or significant cosmetic disfigurement. (◆, ●●)
Rec 5: When systemic therapies are considered for treatment of BCC in GS, the first-line is HHIs, with PD-1 inhibitors to be considered in high-risk disease cases when other systemic therapies have been unsuccessful. (◆, ●●)

Rec 6: When HHIs are used for treatment of BCC in GS, intermittent dosing and treatment holidays may increase tolerability for patients and may result in improved quality of life. (◆, ●●)
Rec 7: Systemic therapy for treating BCC is rarely a standalone intervention for the management of BCC in GS and is typically combined with other modalities. (◆, ●)
Rec 8: When patients who had previously responded to systemic HHIs show signs of oligoprogression, therapy may be continued if it is believed to be slowing progression, and resistant tumors may be treated by other modalities. (◆, ●)
Rec 9: Patients with SUFU mutations should not receive the current generation of smoothened inhibitors for the treatment of BCC in GS, as they are likely to be ineffective. (◆◆, ●)
Rec 10: In patients with BCC in GS, a multimodal treatment approach that includes both lesion-specific and field therapies should be selected based on a therapeutic alliance and joint discussions between pt and physician designed to spare normal tissue, reduce procedural and surgical interventions, include appropriate treatment breaks to minimize treatment fatigue and adverse events, and prioritize pt quality of life. (◆, ●)
Rec 11: Combination of medical and procedural treatments for BCC in GS, and their frequency and intensity, should be individualized to the needs and preferences of the pt, with the frequency and intensity of treatments titrated as appropriate over the lifecycle of the pt. (◆, ●)

GS, Gorlin syndrome; BCC, basal cell carcinoma; 5-FU, 5-fluorouracil; HHIs, hedgehog inhibitors; PD-1, programmed cell death protein 1; SUFU, suppressor of fused homolog.

Strength of recommendation: ◆ Conditional, ◆◆ Strong; Level of evidence: ● Low, ●● Moderate.

Table II. Recommendations for Photodynamic, Laser, Surgical, Destructive, and Radiation Therapies

Rec 12: For patients who can tolerate PDT, this may be considered for treatment of individual lesions; field therapy of low-risk existing BCC; and/or possibly prevention of BCCs in patients with GS. (◆, ●)
Rec 13: To improve treatment effectiveness, prior to PDT for treating BCC in patients with GS, exophytic tumors should be debulked, thick crusts should be removed, and pretreatment with topical medications such as 5-FU or imiquimod may be considered. (◆, ●)
Rec 14: Laser and energy-based devices are not first-line therapies for BCC in GS. Potentially, vascular or ablative lasers may be considered in addition to first-line treatments in low-risk tumors. (◆, ●)
Rec 15: Since the development of BCC in GS can be a continuous and lifelong process, surgical extirpation should be performed judiciously to minimize scarring, functional impairment, and surgical fatigue. (◆, ●)
Rec 16: When BCC in GS are removed surgically, the goal is to obtain clear surgical margins. However, for low-risk tumors, surgery may be stopped before all superficial margins are clear when the alternative is significant disfigurement, functional impairment, or surgical fatigue. (◆, ●)
Rec 17: Reconstruction after removal of BCC in GS should, when possible, be by second intent or linear repair due to the need to: (1) be extremely tissue-sparing given the likelihood of additional future tumors; and (2) avoid transposing adjacent tumors into the defect site. (◆◆, ●)
Rec 18: When procedural interventions are deemed appropriate for children with BCC in GS, preoperative sedation may enable the debulking or removing of many lesions while mitigating pt anxiety, but the risks of sedation should be carefully considered, and the duration of sedation minimized. (◆, ●)
Rec 19: Cryotherapy is not a first-line treatment for BCC in GS. However, cryotherapy may be considered for the treatment of small, superficial, and low-risk BCC. (◆, ●)
Rec 20: When cryotherapy is used to treat BCC in GS, freeze and thaw cycles should be of sufficient duration for tumor destruction and intralesional anesthesia may help ensure pt comfort. (◆, ●)
Rec 21: RT for BCC in GS is absolutely contraindicated in the pediatric population. Among adults, RT is relatively contraindicated and should only be used as a salvage therapy or for palliation for high-risk lesions in older patients when other treatments are contraindicated or infeasible. (◆◆, ●)

GS, Gorlin syndrome; BCC, basal cell carcinoma; 5-FU, 5-fluorouracil; PDT, photodynamic therapy; RT, radiation therapy.

Strength of recommendation: ◆ Conditional, ◆◆ Strong; Level of evidence: ● Low, ●● Moderate.

543 Table III. Recommendations for Monitoring, Prevention, Imaging and Multidisciplinary Care

Rec 22: For patients with BCC in GS, who may have very large numbers of small and asymptomatic lesions and/or who may be suffering from treatment fatigue, treatment may be deferred and instead observation may be a strategy, provided that this is arrived at through shared decision making, keeping in mind that potentially aggressive lesions should be treated to mitigate potential harms. (◆, ●)
Rec 23: To monitor the development of BCC in GS, routine clinical examination may include as appropriate, the use of dermoscopy, serial high-resolution photography and mapping, careful assessment of high-risk areas such as sensory organs (i.e., eyelids, nose, lips, etc.), and asking the pt to localize new onset tumors that they find concerning or symptomatic. (◆, ●)
Rec 24: Patients with GS and their family members and caregivers should be encouraged to monitor the pt's skin at home by serial examination and/or photography, including assessment of hard-to-examine areas, to identify new or concerning tumors. Should such tumors develop before a scheduled clinic visit, patients should consider reaching out to their physician to expedite a visit. (◆, ●)
Rec 25: Patients should be regularly counseled on the protective effects of sun protection and sun avoidance, and frequently reminded of these measures, given the significant lifestyle modifications required for adherence. (◆, ●)
Rec 26: Imaging studies are generally not necessary to delineate BCC in GS but may be appropriate for mapping the extent of deeply invasive BCC that impinge on underlying tissues such as muscle, bone, major vessels, nerves, lymphatics, and other critical structures such as sensory organs. (◆, ●)
Rec 27: When imaging studies are required to assess BCC in GS, modalities should be utilized that minimize ionizing radiation (e.g., ultrasound and/or MRI). (◆◆, ●)
Rec 28: To minimize treatment fatigue, clinical appointments for patients with GS with BCC should whenever possible be consolidated, such that patients have multiple lesions that are growing, symptomatic, or those likely to cause disfigurement or impair function treated at a single visit and/or meet with multiple specialists on the same day. (◆, ●)
Rec 29: Once the diagnosis of GS has been established, the dermatologist or other physician most involved in managing the patients' condition should assist in assembling a multidisciplinary team, whenever possible, at an academic or other well-resourced center for comprehensive lifelong management. (◆, ●)

544 GS, Gorlin syndrome; BCC, basal cell carcinoma; MRI, magnetic resonance imaging.

545 Strength of recommendation: ◆ Conditional, ◆◆ Strong; Level of evidence: ● Low, ●● Moderate.

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547 Table IV. Recommendations for Mental Health, Genetics, Clinical Trials and Special Considerations

Rec 30: Soon after being diagnosed with GS, patients should be referred for mental health screening and services, and encouraged to join pt support groups (e.g., GS Alliance). (◆, ●●)
Rec 31: Genetic testing should be obtained on every pt with suspected GS and clinically diagnosed GS. Whole-exome sequencing is preferred, but disease-specific panels are also acceptable. (◆◆, ●)
Rec 32: Patients with GS should receive genetic counseling focused on family planning. (◆, ●)
Rec 33: Family members of patients with GS should be screened with a history and physical, and if there is clinical suspicion for GS, should receive genetic testing. (◆, ●)
Rec 34: Prenatal testing and diagnosis for GS patients may be considered. (◆, ●)
Rec 35: Patients with BCC in GS should be informed of ongoing clinical trials in which they may be eligible to participate. (◆, ●)
Rec 36: To improve understanding of the epidemiology, disease progression, and treatment response of BCC in GS, all patients should be strongly encouraged to enroll in a clinical data registry. (◆, ●)
Rec 37: For patients who have been diagnosed with GS and received multiple prior skin biopsies with histopathologic findings indicative of BCC, additional BCC may be diagnosed by clinical examination and dermatoscopic findings alone such that biopsy confirmation is infrequently necessary or required prior to treatment. However, in selected cases, when the clinician is uncertain regarding the diagnosis of a particular lesion, biopsy for histopathological confirmation may be obtained prior to treatment with destructive or other modalities. (◆, ●)

Rec 38: The dermatologist caring for the pt with BCC in GS should contact the pt's primary care provider to help educate them on GS, including its clinical manifestations and progression, and keep them apprised of the treatment plan. (◆, ●)

GS, Gorlin syndrome; BCC, basal cell carcinoma.

Strength of recommendation: ◆ Conditional, ◆◆ Strong; Level of evidence: ● Low, ●● Moderate.

Table V. Disease Severity, Lesion Prioritization, Psychosocial Impact, and Financial Burden

Rec 39: Treatment of BCC in GS should be modified to address disease severity, which includes consideration of the number of BCC present, the size of BCC, the rate of growth of BCC, the rate of onset of new BCC, psychosocial impact of BCC on pt well-being, impact of BCC on activities of daily living and employment, functional impairment due to BCC, significant cosmetic disfigurement due to BCC, presence of pathologically aggressive BCC, and presence of deeply invasive or advanced/inoperable/metastatic BCC. (◆, ●)
Rec 40: Cure of all associated skin tumors is generally not a realistic therapeutic goal for patients with BCC in GS. Instead, the optimal outcomes are usually preservation of quality of life and extension of the duration of progression-free survival, defined in the context of GS as maintaining clinical control over BCC lesions to prevent enlargement, deep tissue invasion, or functional/cosmetic morbidity. (◆, ●)
Rec 41: In patients with BCC in GS, individual BCC that may cause functional impairment or cosmetic disfigurement; or large or high-risk lesions that pose a significant risk of metastasis or mortality; must be treated promptly and definitively even in patients who otherwise have mild disease. (◆, ●)
Rec 42: When treating BCC in GS, particular consideration should be directed at minimizing scarring since accumulated scarring over time can result in profound disfigurement, functional impairment, and psychological burden. (◆, ●)
Rec 43: In patients with BCC in GS, when multiple individual BCC require treatment, symptomatic lesions and those at risk of becoming inoperable or metastatic should be treated first. (◆, ●)
Rec 44: Upon diagnosis of children with BCC in GS, comprehensive education should be provided to their families regarding the importance of minimizing environmental exposure to UV light and radiation sources to reduce BCC tumor growth. (◆, ●)
Rec 45: Shared decision making involving the pt, their family, and their medical team should be implemented to develop a treatment plan that meets the pt's goals to minimize the current and future BCC tumor burden in GS, while mitigating treatment fatigue and associated psychosocial distress. (◆, ●)
Rec 46: The appearance of "skin tags" or multiple dark brown papules which are not typical nevi in a child should trigger immediate skin biopsy with histopathologic examination by a dermatopathologist as this could be a sentinel event leading to the diagnosis of GS. (◆◆, ●)
Rec 47: Physicians treating patients with BCC in GS should be aware that patients face a lifelong financial burden of direct and indirect medical costs, which physicians should attempt to mitigate whenever possible by selecting lower-cost treatments and seeking subsidies and alternative sources of financial support. (◆, ●)

GS, Gorlin syndrome; BCC, basal cell carcinoma.

Strength of recommendation: ◆ Conditional, ◆◆ Strong; Level of evidence: ● Low, ●● Moderate.

Supplementary Table I. Composition and Participation of Expert Panel and Patient Representatives

https://data.mendeley.com/datasets/sfymg5h76b/1/files/22e01dc1-15b0-40cd-998f-14fe8ddd67b2

Supplementary Table II. Search Strategy for Systematic Review

https://data.mendeley.com/datasets/sfymg5h76b/1/files/9cf29870-90a9-4083-9c5d-dc26231c16e6

Supplementary Table III: Supplementary Table III. Expert Evidence Survey

https://data.mendeley.com/datasets/sfymg5h76b/1/files/abb90711-7a78-45be-8c4d-c7ddb8cf1914

Supplementary Table IV: Supplementary Table IV. Structured Patient Interview Questions for Basal Cell Carcinoma in Gorlin Syndrome
https://data.mendeley.com/datasets/sfymg5h76b/1/files/d71e7279-92b0-47e8-a33b-bae4dd4edbde

Supplementary Figure I: Comparison to Guidelines for Sporadic BCC and Justification for Gorlin Syndrome-Specific Modifications
https://data.mendeley.com/datasets/sfymg5h76b/1/files/22e01dc1-15b0-40cd-998f-14fe8ddd67b2

Supplementary Figure II: Study Selection Flow Diagram for Systematic Review of BCC Management in Gorlin Syndrome
https://data.mendeley.com/datasets/sfymg5h76b/1/files/8612184d-688e-4538-936f-9b33d89a76ab

Supplementary Figure III: Delphi Consensus and Recommendation Development Process
https://data.mendeley.com/datasets/sfymg5h76b/1/files/b33e759f-4c46-4e41-a53e-ecc1728de566

Supplementary Figure IV: Surgical Approaches
https://data.mendeley.com/datasets/sfymg5h76b/1/files/f27da1f8-f9cf-4360-b50b-d05b7a100239