



ADVANCED BCC POCKET GUIDE

WHEN SYSTEMIC THERAPY IS AN OPTION

A Quick Reference for Clinicians



Risk Factors for Recurrence



LOW RISK

- ✓ <2 cm on trunk/extremities
- ✓ Well-defined borders
- ✓ Primary
- ✓ Nodular, superficial, and other non-aggressive growth patterns

HIGH RISK

- ✓ ≥2 cm on trunk/extremities
- ✓ Head, face, neck, hands, feet, pretibial, and anogenital area (any size)
- ✓ Poorly defined borders
- ✓ Recurrent tumor or prior RT at site
- ✓ Immunosuppression (eg, SOTR)
- ✓ Aggressive subtype (infiltrative, morpheaform, basosquamous, micronodular)
- ✓ PNI

NCCN® stratifies BCC into low- and high-risk groups to determine optimal local treatment options to reduce risk

BCC rarely metastasizes, so no single system (AJCC-8, BWH) perfectly predicts outcomes—risk stratification guides surveillance and treatment intensity rather than dictating a single path

The BWH BCC system is validated and most appropriate for predicting risk of metastasis or death

When Tumors Are Advanced: ACT



Consider imaging (CT/MRI) for perineural or deep-tissue involvement in higher-stage (BWH T2) disease



Consider systemic therapy: HHI (vismodegib/sonidegib) 1L for locally advanced/metastatic disease not curable by surgery or radiation; cemiplimab reserved for progression on or intolerance to HHI



Do NOT manage BWH T2 (high-risk) disease with surgery alone—10-year cumulative metastasis/death risk is 37% vs 0 in T1



Collaborate with a multidisciplinary team—Mohs/dermatologic surgery, radiation oncology, and medical oncology as indicated

When to Refer



laBCC: primary or recurrent extensive disease for which surgery and/or RT may not be curative or would cause significant functional/cosmetic impairment



Nodal or metastatic disease: any regional nodal or distant metastasis; rare, but requires systemic therapy and multidisciplinary management



HHI candidate or failure: advanced BCC for 1L HHI (vismodegib/sonidegib) OR progression/intolerance warranting 2L cemiplimab



Aggressive or deeply invasive tumors: basosquamous, infiltrative, morpheaform, or sarcomatoid subtypes; bone, named-nerve, or deep soft-tissue involvement



Genetic syndromes: basal cell nevus (Gorlin) syndrome or xeroderma pigmentosum—refer for genetic evaluation and consider systemic/surveillance strategies



Multidisciplinary decision needed: when treatment choice spans surgery, RT, HHIs, immunotherapy, or clinical trials, tumor board input is strongly encouraged



Most BCCs are cured locally, but advanced disease needs systemic therapy and multidisciplinary coordination.

1L, first-line; 2L, second-line; AJCC-8, American Joint Committee on Cancer, 8th edition; BCC, basal cell carcinoma; BWH, Brigham and Women's Hospital; CT, computed tomography; CV, cardiovascular; HHI, hedgehog inhibitor; laBCC, locally advanced BCC; NCCN, National Comprehensive Cancer Network; MRI, magnetic resonance imaging; PNI, perineural involvement; RT, radiation therapy; SOTR, solid organ transplant recipient; T, tumor.

Drobní ZD, et al. *Circulation*. 2020;142(24):2299-2311; Morgan FC, et al. *J Am Acad Dermatol*. 2021;85(3):582-587; NCCN. 2026. https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf; Peris K, et al. *Eur J Cancer*. 2023;192:113254.



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When to Consider Immunotherapy for Advanced BCC



	Preferred	Other Recommended	Useful in Certain Circumstances
Locally Advanced Disease—Neoadjuvant	None	• Vismodegib ^a (category 2B ^b)	• Cemiplimab-rwlc ^d (category 2B ^b)
Locally Advanced Disease	None	• Sonidegib • Vismodegib ^c	• Cemiplimab-rwlc ^d
Nodal Disease	None	• Vismodegib • Sonidegib (category 2B ^b)	• Cemiplimab-rwlc ^d
Metastatic Disease	Vismodegib	• None	• Cemiplimab-rwlc ^d

FDA-Approved HHIs and ICIs for Advanced BCC

	Vismodegib ^e	Sonidegib ^e	Cemiplimab-rwlc ^f
Target/Class	HHI	HHI	Anti-PD-1/Human IgG4 mAb
BCC Indication	Adults with mBCC, or laBCC recurring after surgery, or in those who are not candidates for surgery/RT	Adults with laBCC recurring after surgery/RT or those who are not candidates for surgery/RT	Adults with laBCC or mBCC previously treated with an HHI or for whom an HHI is not appropriate
Monitoring	Obtain baseline serum CPK and creatinine levels and as clinically indicated	Obtain serum CK and creatinine levels prior to initiating therapy, periodically during treatment, and as clinically indicated	Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment

CK, creatine kinase; CPK, creatine phosphokinase; FDA, US Food and Drug Administration; ICI, immune checkpoint inhibitor; IgG, immunoglobulin G; mAb, monoclonal antibody; mBCC, metastatic BCC; PD-1, programmed cell death protein 1.

^aIn one study of 55 patients with laBCC, neoadjuvant administration of vismodegib before planned surgery allowed for a smaller surgical procedure in 71% of patients, although it carried a high (36.4%) recurrence risk; ^bCategory 2B indicates that the recommendation is based upon lower-level evidence, but there is NCCN[®] consensus that the intervention is appropriate (≥50%, but <85% support of the panel); ^cIn certain circumstances, RT can be combined with vismodegib;

^dCemiplimab-rwlc is FDA approved for patients with laBCC or mBCC previously treated with an HHI or for whom an HHI is not appropriate; the role of adjuvant systemic therapy for resected BCC is unclear and, thus, it is best performed in a clinical trial setting; ^eDue to the frequency of intolerable side effects associated with HHIs, drug holidays or other alternatives to daily dosing can be used to reduce side effects to improve adherence to therapy and quality of life; ^fNCCN Guidelines[®] also recommend cemiplimab (in certain circumstances) for neoadjuvant treatment of laBCC.

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