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Non-excisional management of non-melanoma skin cancer (NMSC)

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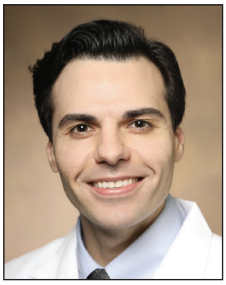

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This guide focuses on high-yield alternatives to Mohs micrographic surgery and wide local excision (WLE) for low-risk, field-cancerized, or advanced disease. While surgical excision and Mohs remain the gold standard for most non-melanoma skin cancers (NMSC), a non-excisional approach is often the "next best step" in specific clinical scenarios. Non-excisional modalities are generally favored for superficial or well-differentiated histologies located on low-risk sites (trunk and extremities). Conversely, high-risk pathologic features, "H-zone" locations, or immunosuppression should prompt a shift toward definitive surgical margins. This guide provides a high-yield framework for navigating these alternatives, ranging from destructive in-office procedures to advanced systemic therapies.

Destructive & light-based modalities

Modality	Best indication	Mechanism/protocol	Board high-yield "watch out"
Electrodesiccation & curettage	Low-risk BCC/SCC on trunk/extremities	Typically, 3 cycles of "scrape and burn"	Contraindicated in terminal hair-bearing areas (follicular extension of tumor)
Cryosurgery	Small, superficial BCC/ squamous cell carcinoma in situ (SCCis)	Liquid nitrogen to create ice ball. Rapid freeze to at least -50°C and slow thaw	Risk of dyspigmentation and scarring
Photodynamic therapy (PDT)	Superficial BCC	Singlet oxygen production via light + photosensitizer (ALA + blue light/MAL + red light)	Avoid in photosensitizing conditions (i.e., porphyria, XP, etc.)

Topical & intralesional (IL) procedures

Agent	Indications	Role in therapy	Mechanism	Clinical pearl
Topical 5-FU	Small tumors (typically < 2cm), low-risk sites (trunk, extremities)	Superficial BCC, SCCis	Inhibits thymidylate synthase in rapidly dividing tumor cells	Brisk inflammation is a sign of efficacy; S-phase specific
Topical imiquimod	Small tumors (typically < 2cm), low-risk sites (trunk, extremities)	Superficial BCC, SCCis	TLR-7 agonist; induces IFN-alpha	Can cause flu-like symptoms due to cytokine release
IL 5-FU (off-label)	Poor surgical candidates and tumors in cosmetically sensitive areas	Keratoacanthoma; select SCCs	Antimetabolite; inhibits thymidylate synthase in rapidly dividing tumor cells	Rapid involution; useful for lesions on low-laxity or poor-healing sites where surgery is undesirable
IL methotrexate (off-label)	Poor surgical candidates and tumors in cosmetically sensitive areas	Keratoacanthoma; select SCCs	Dihydrofolate reductase inhibitor	Useful alternative if 5-FU is contraindicated
IL bleomycin-electrochemotherapy (ECT)	Poor surgical candidates and tumors in cosmetically sensitive areas	KAs, well-differentiated SCCs, and BCCs	DNA strand breaks (G2/M arrest)	Superior efficacy to IL 5-FU and IL MTX but injections are more painful and requires access to specialized equipment (electrodes, pulse generator)

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Systemic chemoprevention & advanced therapy

Category	Agent	Target population	Mechanism	Board "must-knows"
Chemoprevention (prevents *new* tumors)	Acitretin	Solid organ transplant recipients and other very high-risk SCC patients (e.g., xeroderma pigmentosum)	RAR/RXR agonist; normalizes keratinocyte differentiation.	Rebound SCC flare if discontinued; monitor lipids and LFTs; teratogenic—avoid pregnancy for 3 years after stopping (drug persists longer with alcohol use)
Chemoprevention (prevents *new* tumors)	Capecitabine	Solid organ transplant recipients with high tumor burden	Oral prodrug of 5-FU; converted by thymidine phosphorylase	Must screen for dihydropyrimidine dehydrogenase deficiency to avoid toxicity
Chemoprevention (prevents *new* tumors)	Nicotinamide (vitamin B3)	High-risk patients with prior NMSC (non-transplant)	Facilitates ATP production; enhances DNA repair	Dose 500 mg BID; no flushing (unlike niacin); reduces new SCCs and BCCs by ~20–30%
Chemoprevention (prevents *new* tumors)	Sirolimus, everolimus	Solid organ transplant recipients with prior NMSC	mTOR inhibitor	Switching from calcineurin inhibitors to mTOR inhibitors reduces SCC development
Therapeutic (treats *existing* tumors)	Hedgehog pathway inhibitors (SMO inhibitors: e.g., vismodegib, sonidegib)	Locally advanced or metastatic BCC not amenable to surgery or radiation	Inhibits Smoothened (SMO) in the sonic hedgehog signaling pathway	Characteristic adverse effects: dysgeusia/ageusia, muscle cramps, alopecia, weight loss
Therapeutic (treats *existing* tumors)	PD-1 inhibitors (e.g., cemiplimab, pembrolizumab)	Locally advanced, recurrent, or metastatic SCC not amenable to surgery or radiation: BCC if failed SMO inhibitor or SMO inhibitor contraindicated	PD-1 blockade restores antitumor T-cell activity	Reserved for unresectable disease; monitor for immune-related adverse events (e.g., colitis, thyroiditis)

References:

1. Mariwalla, K., & Leffell, D. J. (2011). *Primer in dermatologic surgery: A study companion* (2nd ed.). American Society for Dermatologic Surgery.
2. Bolognia, J. L., Schaffer, J. V., & Cerroni, L. (2024). *Dermatology* (5th ed.). Elsevier.
3. Stewart JR, Lang ME, Brewer JD. Efficacy of nonexcisional treatment modalities for superficially invasive and in situ squamous cell carcinoma: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2022;87(1):131-137. doi:10.1016/j.jaad.2021.07.067.
4. Chitwood K, Etzkorn J, Cohen G. Topical and intralesionawl treatment of nonmelanoma skin cancer: efficacy and cost comparisons. *Dermatol Surg*. 2013;39(9):1306-1316. doi:10.1111/dsu.12300.
5. Good LM, Miller MD, High WA. Intralesional agents in the management of cutaneous malignancy: a review. *J Am Acad Dermatol*. 2011;64(2):413-422. doi:10.1016/j.jaad.2009.12.013.
6. Breglio KF, Knox KM, Hwang J, et al. Nicotinamide for Skin Cancer Chemoprevention. *JAMA Dermatol. 2025;161(11):1140–1147. doi:10.1001/jamadermatol.2025.3238.*
7. Bik L, Sangers T, Greveling K, Prens E, Haedersdal M, van Doorn M. Efficacy and tolerability of intralesional bleomycin in dermatology: A systematic review. *J Am Acad Dermatol*. 2020 Sep;83(3):888-903.
8. Heller R, Jaroszeski MJ, Reintgen DS, Puleo CA, DeConti RC, Gilbert RA, Glass LF. Treatment of cutaneous and subcutaneous tumors with electrochemotherapy using intralesional bleomycin. *Cancer*. 1998 Jul 1;83(1):148-57.