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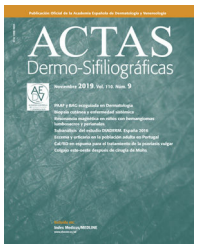

RESIDENT'S FORUM

[Translated article] RF – Intralesional 5-Fluorouracil in the Treatment of Nonmelanoma Skin Cancer

FR – Tratamiento intralesional del cáncer cutáneo no melanoma con 5-fluorouracilo

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PALABRAS CLAVE
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Nonmelanoma skin cancer (NMSC) includes cutaneous squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). It is the most common cancer in humans and ranks fifth in terms of economic burden.[1,2]

The treatment of choice is surgery,[3–5] but nonsurgical options can be contemplated in selected cases. Intralesional chemotherapy, for example, has been used off label for more than 50 years. The agents include 5-fluorouracil (5-FU) (Table 1), methotrexate, bleomycin, and interferon-α.[3,4]

In 2021, Maxfield et al.[4] published the largest study to date on the use of intralesional 5-FU in SCC. It was a retrospective cohort study of 148 patients with a median age of 74 years and 172 tumors: 164 invasive SCCs and 8 keratoacanthomas. The most common location was the lower extremities (37%). Between 0.2 and 2 mL of 5-FU was injected at a concentration of 50 mg/mL into the base of the tumors following the administration of lidocaine 1% and adrenaline 1:100 000 to anesthetize the area. In total, 92% of the tumors (158/172) showed a complete response, and just 1 dose was needed in 76% of cases. The remaining 24% required at least 2 doses, generally administered 4 weeks apart. The 14 tumors that did not respond were treated surgically without complications. Just 1 recurrence (keratoacanthoma) was observed after a median follow-up of 9.5 months. None of the patients developed moderate or severe adverse effects.

2021 also saw the publication of a systematic review on the use of intralesional 5-FU in NMSC.[5] The authors analyzed 19 studies involving 283 patients. The complete response

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Table 1 Intralesional Treatment of Nonmelanoma Skin Cancer With 5-Fluorouracil.[a]

Drug	Mechanism of action	Dose	Administration interval	Complete response rate	Contraindications	Adverse effects
5-Fluorouracil	Uracil analog DNA and RNA alterations	50 mg/mL (0.5–2 mL)	4 wk[b]	BCC > 90% SCC: ≈ 90% Keratoacanthoma: 76%–98%	Severe liver disease Pregnancy or breastfeeding	Local: pain, erythema, erosion, necrosis Systemic (rare): cytopenia, gastrointestinal effects

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma.
[a] Histologic confirmation is recommended before any nonsurgical treatment.
[b] Most tumors (76%) resolved after just 1 injection.

rate was higher in SCC (87%) and BCC (91.4%) than in keratoacanthoma (74.5%, $P = .007$), and the times to resolution were similar (9–12 weeks). Previous systematic reviews had shown similar results.[1,3] Most of the BCCs were low risk (<15 mm, superficial or nodular), although aggressive subtypes (multifocal, recurrent, morpheaform) also responded. In the different studies reviewed, a volume ranging from 0.5 to 2 mL (depending on tumor size) was injected at a concentration of 15–25 mg/mL, with a mean of 4–8 injections and a cumulative mean dose of 90 mg (up to 612 mg in recurrent cases). The patients were followed for between 12 and 24 weeks. The most common adverse effects were local, transient reactions (erythema, edema, erosion, ulceration). None of the patients experienced hematologic or systemic adverse effects.[1]

Although surgery remains the treatment of choice for NMSC, intralesional 5-FU may be an effective, safe, and minimally invasive treatment for patients with a high surgical risk or who have tumors in complex locations or do not wish surgery. Its use as a neoadjuvant agent should be explored in clinical studies.

References

1. Metterle L, Nelson C, Patel N. Intralesional 5-fluorouracil (FU) as a treatment for nonmelanoma skin cancer (NMSC): a review. J Am Acad Dermatol. 2016;74:552–7.
2. Chitwood K, Etzkorn J, Cohen G. Topical and intralesional treatment of nonmelanoma skin cancer: efficacy and cost comparisons. Dermatol Surg. 2013;39:1306–16.
3. Kirby JS, Miller CJ. Intralesional chemotherapy for nonmelanoma skin cancer: a practical review. J Am Acad Dermatol. 2010;63:689–702.
4. Maxfield L, Shah M, Schwartz C, Tanner LS, Appel J. Intralesional 5-fluorouracil for the treatment of squamous cell carcinomas. J Am Acad Dermatol. 2021;84:1696–7.
5. Maghfour J, Kuraitis D, Murina A. Intralesional 5-fluorouracil for treatment of non-melanoma skin cancer: a systematic review. J Drugs Dermatol. 2021;20:192–8.