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SQUAMOUS CELL CARCINOMA OF THE SKIN

Ana Belén Valero Martillo[1], Alejandra Gabriela Villa García[2], Bryam Esteban Coello García[3].

[1]*General Practitioner at "Cesfarm Dr. Edelberto Elgueta", faculty of Medical Sciences, Universidad de Cuenca. Ciudad de Melipilla, Región Metropolitana de Santiago. Chile. ORCID https://orcid.org/0000-0002-7123-1805*
[2]*General Practitioner at "Hospital Monte Sinaí",faculty of Medical Sciences, Universidad de Cuenca. Azuay- Ecuador ORCID https://orcid.org/0009-0001-0581-4113*
[3]*Postgraduate doctor in orthopedics and traumatology at Faculdade de Ciências Médicas Minas Gerais. Belo Horizonte - Brasil. ORCID https://orcid.org/0000-0003-2497-0274*

Corresponding Author: *Bryam Esteban Coello García,* ***Address:*** *Rua Teresópolis 183. Belo Horizonte. Minas Gerais. Brasil.* ***Postal Code:*** *31130050*

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ABSTRACT

Introduction: *squamous cell carcinoma is steadily increasing year after year, representing a major public health challenge. The mortality rates of dermal squamous cell carcinoma are comparable to those of melanoma, renal carcinoma and oropharyngeal carcinoma. Adequate surveillance, early diagnosis and prompt treatment are essential to reduce the risks of morbidity and mortality.*
Objective: *to detail current information related to cutaneous squamous cell carcinoma, etiology, epidemiology, pathophysiology, histopathology, examination, evaluation, treatment, differential diagnosis, prognosis and complications.*
Methodology: *a total of 37 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 25 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, Google Scholar and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: skin cancer, epidermoid carcinoma, squamous cell, clear cell, Mohs surgery, cutaneous carcinoma.*
Results: *cutaneous squamous cell carcinoma has a multifactorial etiology, with UV radiation being the main risk factor. It is the second most common form of skin cancer in the USA, with a higher incidence in men and fair-skinned, older people. The mortality rate is between 1% and 2%, although in some regions it may be comparable to other more aggressive cancers. It originates from keratinocytes and often has mutations in the tp53 gene. There are several histological subtypes with different characteristics and prognoses. Diagnosis is confirmed by biopsy, and staging is performed with systems such as BWH and AJCC-8, with surgical excision being the preferred intervention.*
Conclusions: *cutaneous squamous cell carcinoma represents an important public health problem, emphasizing the need for prevention and sun protection education programs. Early identification and appropriate treatment are crucial to improve prognosis. The diversity of risk factors, together with the variability in histologic subtypes and their clinical behavior, underscores the importance of a personalized approach to care. In addition, rigorous surveillance is essential in immunocompromised patients, who are at significantly increased risk of developing this neoplasm. Finally, continued research and development of new therapies, such as immunotherapeutic agents, promise to improve clinical outcomes and quality of life for affected patients.*
KEY WORDS: *cancer, carcinoma, skin, squamous, Mohs.*

INTRODUCTION

Squamous cell carcinoma is the second most common dermal malignancy in some countries. Risk factors include immunosuppression, chronic lesions, fair skin, male gender, advanced age, various genetic syndromes, environmental exposure such as UV radiation, and a history of squamous cell carcinoma. Although metastasis is uncommon, the most common site of spread is the lymph nodes. Since the incidence is steadily increasing, representing a significant public health problem, adequate surveillance, early diagnosis and prompt treatment are essential to reduce the risks of morbidity and mortality. Photoprotection and frequent skin checks at body level are suggested. Although most cases are treated with surgical excision, new therapeutic modalities continue to emerge. Systemic oncologic therapy and radiation therapy may be appropriate for more advanced cases(1-4).

Squamous cell carcinoma is steadily increasing year after year, representing a major public health challenge. Mortality rates for dermal squamous cell carcinoma are comparable to those for melanoma, renal carcinoma, and oropharyngeal carcinoma in the central and southern regions of the United States. Skin cancer is a condition with significant frequency worldwide and is generally classified into nonmelanoma skin cancer (NMSC) or melanoma. The exact incidence of skin cancer is complex to determine due to lack of diagnostic criteria and sometimes

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underreporting. However, multiple epidemiological studies have shown an increase in the incidence of both NMSC and melanoma in recent years. The diagnosis and treatment of this type of neoplasm constitutes a very relevant public health problem, especially in relation to patient and health care costs. Skin cancers are usually located in sun-exposed areas of the head and neck, leading to considerable morbidity during diagnosis and treatment. There are various therapeutic options such as cryotherapy, chemotherapy, immunotherapy, surgical excision and radiotherapy. Adequate sun protection is essential for the prevention of skin cancer(5,6).

This article details the current information related to cutaneous squamous cell carcinoma, etiology, epidemiology, pathophysiology, histopathology, examination, evaluation, treatment, differential diagnosis, prognosis and complications.

METHODOLOGY

A total of 37 articles were analyzed in this review, including review and original articles, as well as cases and clinical trials, of which 25 bibliographies were used because the information collected was not important enough to be included in this study. The sources of information were Cochrane, PubMed and Google Scholar; the terms used to search for information in Spanish, Portuguese and English were: skin cancer, epidermoid carcinoma, squamous cell, clear cell, Mohs surgery, cutaneous carcinoma.

The choice of bibliography exposes elements related to cutaneous squamous cell carcinoma; etiology, epidemiology, pathophysiology, histopathology, examination, evaluation, treatment, differential diagnosis, prognosis and complications of the disease are presented.

DEVELOPMENT

Etiology

The development of dermal squamous cell carcinoma is related to the following risk factors and etiologies:
UV radiation: UVA and UVB rays are the most significant risk factors.
Environmental exposures other than UV radiation: This includes arsenic, polycyclic aromatic hydrocarbons, nitrosamines, alkylating agents and ionizing radiation.
Demographic factors: Fair skin, male gender and advanced age.
Immunosuppressed state: Iatrogenic, leukemia and AIDS.
Genetic syndromes: Huriez syndrome, xeroderma pigmentosum, oculocutaneous albinism, dyskeratosis congenita, Rothmund-Thomson syndrome, Werner syndrome, Bloom syndrome, dystrophic epidermolysis bullosa, epidermodysplasia verruciformis, Fanconi anemia, keratitis-ichthyosis-deafness syndrome and genetic immunodeficiency syndromes.
Pre-existing lesions: Chronic wounds (Marjolin's ulcer), human papillomavirus, actinic keratosis, porokeratosis, lichen sclerosus and atrophic lichen, hypertrophic or oral lichen planus and discoid cutaneous lupus erythematosus.
Medications: BRAF inhibitors, vismodegib and voriconazole, and immunosuppressive agents(7-9).

Epidemiology

Incidence and Growth:
Squamous cell carcinoma is the second most common form of skin cancer in the United States, underscoring its public health relevance.
A nearly threefold increase in its incidence from the 1970s to the early 2000s is cited, indicating an alarming trend that may reflect changes in exposure to risk factors, such as UV radiation.
Incidence Statistics:
Figures of 140 cases per 100,000 men and 50 per 100,000 women in 2012 suggest that men have a higher risk of developing this neoplasm. This may be related to sun exposure habits or differences in seeking medical care.
Mortality Rate:
The mortality rate of squamous cell carcinoma, which is between 1 % and 2 %, is relatively low compared to other types of cancer, suggesting that, although the disease is common, it may be treatable if detected early.
However, it is noted that in certain regions of the country, mortality resembles that of other more aggressive cancers, such as melanoma, which may indicate a greater aggressiveness of the disease in those geographic settings.
Risk Factors:
The higher prevalence in men, people with fair skin, and older age groups highlights the importance of demographic factors in susceptibility to squamous cell carcinoma. This may be related to cumulative sun exposure and immune response in older populations.
Public Health Implications:
The increased incidence and relevance of squamous cell carcinoma highlights the need for prevention programs, sun protection education, and early detection. This is crucial to address the public health problem posed by this disease(1,10).

Pathophysiology

Origin of Carcinoma:
Cutaneous squamous cell carcinoma originates from keratinocytes, which points to the importance of this cell in the skin and its fundamental role in the formation of this neoplasm.
Genetic Abnormality:
Mutation in the tumor suppressor gene tp53 is identified as the most common genetic abnormality in squamous cell carcinoma and its precursor, actinic keratosis. This highlights the relevance of genetic alterations in cancer pathogenesis and suggests that monitoring for this mutation could be key to early detection and prevention.
Immunosurveillance:
Decreased immunosurveillance in immunosuppressed patients may favor tumor growth. This aspect is critical, as it implies that the immune system's ability to detect and destroy abnormal cells is compromised in certain individuals, increasing their risk of cancer.
Risk in Immunosuppressed Patients:
The data on solid organ transplant patients receiving immunosuppressive therapy, who have a risk of developing squamous cell carcinoma 65 to 250 times higher than the general population, emphasizes the severity of immunosuppression. This suggests that prevention and

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surveillance strategies should be especially rigorous in these patients(2).

Histopathology

Subtype Classification:

There are several histologic subtypes of squamous cell carcinoma, indicating the heterogeneity of this neoplasm. Each subtype may have different clinical features, prognoses and responses to treatment, which is crucial for personalized patient care.

Histologic Description:

These tumors are composed primarily of atypical keratinocytes that exhibit eosinophilic or pink cytoplasm and a vitreous appearance. This description provides valuable information for pathologists and clinicians, aiding in identification and diagnosis through histologic analysis.

Common Findings:

Mention of additional features, such as parakeratosis, intercellular bridges, and keratin beads, reinforce the understanding of squamous cell carcinoma morphology. These findings are helpful to pathologists in histologic evaluation and in establishing an accurate diagnosis.

High-Risk Subtypes:

High-risk subtypes include acantholytic, sarcomatoid, and desmoplastic. Identifying these subtypes is critical, as they may be associated with a higher potential for aggressiveness, recurrence and metastasis, which influences therapeutic decisions and patient prognosis.

Squamous Cell Carcinoma in situ.

This subtype, also called Bowen's disease, is distinguished by full-thickness keratinocyte atypia that has not invaded beyond the basal layer of the epidermis. In contrast, invasive squamous cell carcinoma has penetrated the basal layer. The basal layer usually remains intact, forming the “eyeliner sign”.

Acantholytic/Adenoid/Pseudoglandular

This subtype is distinguished by grooves around clusters or filaments of robust polygonal neoplastic cells, producing a glandular appearance. The groove is a consequence of a desmosomal alteration. Unlike tumors of true glandular origin, such as adenosquamous carcinoma, carcinoembryonic antigen (CEA) staining is negative.

Clear Cell

This subtype is distinguished by clear or faint neoplastic cells that may or may not have an epidermal connection. Histologic differential diagnoses include clear cell acanthoma and renal cell carcinoma.

Spindle/Sarcomatoid Cells

This subtype is distinguished by spindle-shaped keratinocytes with pleomorphic nuclei randomly distributed throughout the dermis in a typically infiltrative pattern (see Image. Histologic slide of squamous cell carcinoma, sarcomatoid). Numerous mitotic figures can be observed. Atypical fibroxanthoma is a significant histologic differential diagnosis that typically stains negative for p63 and p40, unlike spindle cell or sarcomatoid squamous cell carcinoma (see Image. Histological slide of squamous cell carcinoma, staining positive for p40). Immunohistochemistry with p40 is more specific than that with p63.

Desmoplastic

This subtype may resemble the sarcomatoid or spindle cell variant of squamous cell carcinoma. However, desmoplastic carcinoma is characterized by desmoplastic (densely collagenous) stroma in more than 30% of the tumor. Perineural invasion is frequently reported. Desmoplastic melanoma is also included in the histologic differential diagnosis. Unlike desmoplastic melanoma, desmoplastic squamous cell carcinoma usually stains positive for p63 and negative for SOX10 and S100.

Keratoacanthoma

It is distinguished by a crateriform invagination filled with keratin (see image. Histologic slide of squamous cell carcinoma, keratoacanthoma). The neoplastic cells are usually well differentiated.

Verrucous Carcinoma

Distinguished by a verruciform acanthosis with blunt, broad projections that press into the dermis rather than infiltrate it. The cytomorphology associated with human papillomavirus in warty carcinoma is less pronounced compared to benign warts(4,11-13).

Physical Examination and Evaluation

Cutaneous squamous cell carcinoma is typically characterized by a scaly, erythematous or hyperpigmented papule or plaque. Some cases may present with ulceration, fungal features, or pain (see Image. Cutaneous squamous cell carcinoma). Because of its strong association with exposure to UV radiation, many cases appear on sun-damaged skin. This tumor can also develop from pre-existing lesions such as actinic keratosis, chronic wounds (Marjolin's ulcer), human papillomavirus infection, porokeratosis, lichen sclerosus and atrophic lichen, hypertrophic or oral lichen planus and discoid cutaneous lupus erythematosus(14-16).

To confirm the diagnosis of cutaneous squamous cell carcinoma, a skin biopsy is necessary. In addition, sentinel lymph node biopsy or radiologic evaluation for lymph node metastases by computed tomography or ultrasound is advised for cases classified as stage T2B-T3 according to the Brigham and Women's Hospital (BWH) staging system or stage T4 according to the American Joint Committee on Cancer, 8th edition (AJCC-8) staging system. For AJCC-8 stages T2-3, it is essential to evaluate each case on an individual basis. For patients with palpable lymphadenopathy, fine needle aspiration or lymph node biopsy is recommended(1,2).

Staging

The staging categories for cutaneous squamous cell carcinoma according to BWH and AJCC-8 are forthcoming.

BWH staging system

Stage T1: 0 high-risk characteristics

Stage T2A: 1 high-risk feature

Stage T2B: 2 to 3 high-risk features

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Stage T3: 4 or more high-risk features or bone invasion
High-risk features, as defined by BWH, include:
Tumor diameter of at least 2 cm.
Histologically poor differentiation
Perineural invasion of at least 0.1 mm
Invasion beyond the subcutaneous tissue
AJCC-8 staging system

Stage Ti: In situ
Stage T1: tumor diameter less than 2 cm
Stage T2: tumor diameter 2 to 3.9 cm
Stage T3:
Tumor diameter of at least 4 cm.
Mild bone erosion
Perineural invasion of at least 0.1 mm or invasion of a nerve located deeper than the dermis.
Invasion beyond the subcutaneous tissue
Invasion greater than 6 mm in depth
Stage T4A: macroscopic invasion of cortical bone or bone marrow
Stage T4B: Invasion of the skull or involvement of the foramen at the base of the skull(1,2)
Treatment.
The preferred therapeutic intervention for cutaneous squamous cell carcinoma is surgical excision. Mohs micrographic surgery is considered the ideal choice in cases that meet appropriate use criteria (AUC). Factors mentioned in the AUC include, but are not limited to, a clinical diameter of the visible lesion greater than 2 cm, high-risk histologic features, recurrent versus primary lesions, cosmetically sensitive and/or high-risk anatomic locations, such as the ears, lips, nose and periocular areas, as well as immunosuppression.

The reported 5-year recurrence rate for Mohs micrographic surgery is about 3.1%, while standard excision with 4 to 6 mm margins has a recurrence rate of about 8.1%. Mohs micrographic surgery provides significantly greater risk reduction compared with standard excision, especially in cases with high-risk features. For example, locally recurrent (previously treated) lesions showed a recurrence rate of 10% with Mohs micrographic surgery and 23.3% with standard excision. Electrodesiccation and curettage are alternative options for in situ cases, although they have slightly higher recurrence rates compared to Mohs micrographic surgery and standard excision(1,17,18).

For patients who are not suitable for surgery, options for treating cutaneous squamous cell carcinoma include superficial radiation therapy, 5-fluorouracil cream, imiquimod cream, cryotherapy, photodynamic therapy and/or ablative laser. However, these treatments often result in higher recurrence rates and lack histologic clearance confirmation. Lymphadenectomy of the associated nodal basin is recommended for lymph node-positive cases.
Radiation therapy is typically used in cases involving large caliber nerve invasion, lymphovascular invasion, multiple lymph nodes or extracapsular extension. Adjuvant systemic oncologic therapy for advanced cases may include chemotherapy, epidermal growth factor inhibitors, or immunotherapy. Recently, new immunotherapeutic agents have emerged that show superior clinical results compared to traditional systemic therapies(19,20).

Differential Diagnosis
There are several, the most notable of which are mentioned below:
Actinic keratosis.
Seborrheic keratosis.
Basal cell carcinoma.
Melanoma.
Lichen planus.
Lichen sclerosus and atrophic lichen.
Discoid cutaneous lupus erythematosus.
Extramammary Paget's disease.
Porokeratosis.
Lichen planus-like keratosis.
Verruca.
Psoriasis.
Nummular dermatitis(21-23).

Prognosis
The prognosis of localized disease is generally excellent. The overall mortality rate for cutaneous squamous cell carcinoma is approximately 1% to 2%, with about 3% of cases developing metastases. Lymph nodes are the most common site of metastasis. Cases involving single node metastases up to 3 cm are associated with a 5-year disease-specific survival of 90%(24,25).

Complications
Pain: indicates the physical suffering that the patient may experience. Pain management is crucial in oncologic treatment, as it affects quality of life.

Loss of function: this may refer to the inability to perform daily activities due to the disease or its treatments. This also suggests the importance of rehabilitation and functional support in cancer patients.

Metastasis: the spread of cancer to other organs is an indicator of disease progression. Metastasis complicates treatment and is generally associated with a worse prognosis.

Local invasion: this refers to how the tumor can spread to surrounding tissues, which can result in additional complications and more complex management.

Poor cosmesis: this points to the cosmetic effects of the disease and its treatment, which can have a significant psychological impact on the patient, affecting their self-esteem and quality of life.

Death: this is the most serious outcome and reflects the severity of the disease. Mortality rate and prognosis are essential considerations in treatment decision making.

RESULTS
Cutaneous squamous cell carcinoma presents a multifactorial etiology, where UV radiation emerges as the main risk factor, associated with an increase in the incidence of the disease since

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the 1970's. Epidemiology indicates that it is the second most common form of skin cancer in the United States, with a markedly higher incidence in men and in individuals with fair skin and advanced age. Epidemiology indicates that it is the second most common form of skin cancer in the United States, with a markedly higher incidence in men and in individuals with fair skin and advanced age. The mortality rate is between 1% and 2%, although in certain regions it may be comparable to that of other more aggressive cancers. The pathophysiology reveals that this carcinoma originates from keratinocytes and is frequently associated with mutations in the tumor suppressor gene tp53. Histologically, several subtypes are identified, each with distinct features and prognoses. Diagnosis is confirmed by biopsy, and staging is performed with systems such as BWH and AJCC-8, which determine the appropriate treatment, with surgical excision being the preferred intervention.

CONCLUSIONS

Cutaneous squamous cell carcinoma represents an important public health problem, emphasizing the need for prevention programs and sun protection education. Early identification and appropriate treatment are crucial to improve prognosis. The diversity of risk factors, together with the variability in histologic subtypes and their clinical behavior, underscores the importance of a personalized approach to care. In addition, rigorous surveillance is essential in immunocompromised patients, who are at significantly increased risk of developing this neoplasm. Finally, continued research and development of new therapies, such as immunotherapeutic agents, promise to improve clinical outcomes and quality of life for affected patients.

BIBLIOGRAPHY

1. *Hadian Y, Howell JY, Ramsey ML. Cutaneous Squamous Cell Carcinoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 2]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK441939/*
2. *Que SKT, Zwald FO, Schmults CD. Cutaneous squamous cell carcinoma. J Am Acad Dermatol. 2018 Feb;78(2):237–47.*
3. *Omland SH, Ahlström MG, Gerstoft J, Pedersen G, Mohey R, Pedersen C, et al. Risk of skin cancer in patients with HIV: A Danish nationwide cohort study. J Am Acad Dermatol. 2018 Oct;79(4):689–95.*
4. *Caudill J, Thomas JE, Burkhart CG. The risk of metastases from squamous cell carcinoma of the skin. Int J Dermatol. 2023 Apr;62(4):483–6.*
5. *Bryam Esteban Coello García, Eliana Maitee Sánchez Gómez, Estefanny Dayana Villafuerte Ruiz, Byron Fabián Pinos Reyes, Rossanny Cecilia Gómez González, Cecibel Carolina Mogrovejo Zúñiga, et al. SKIN CANCER SCOPING REVIEW. EPRA Int J Multidiscip Res IJMR. 2024 Jul 25;371–4.*
6. *Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence Estimate of Nonmelanoma Skin Cancer (Keratinocyte Carcinomas) in the U.S. Population, 2012. JAMA Dermatol. 2015 Oct;151(10):1081–6.*
7. *Coggshall K, Farsani T, Ruben B, McCalmont TH, Berger TG, Fox LP, et al. Keratitis, ichthyosis, and deafness (KID) syndrome: A review of infectious and neoplastic complications. J Am Acad Dermatol. 2013 Jul;69(1):127-134.e3.*
8. *Jaju PD, Ransohoff KJ, Tang JY, Sarin KY. Familial skin cancer syndromes. J Am Acad Dermatol. 2016 Mar;74(3):437–51.*
9. *Bleeker MCG, Visser PJ, Overbeek LIH, Van Beurden M, Berkhof J. Lichen Sclerosus: Incidence and Risk of Vulvar Squamous Cell Carcinoma. Cancer Epidemiol Biomarkers Prev. 2016 Aug 1;25(8):1224–30.*
10. *Muzic JG, Schmitt AR, Wright AC, Alniemi DT, Zubair AS, Olazagasti Lourido JM, et al. Incidence and Trends of Basal Cell Carcinoma and Cutaneous Squamous Cell Carcinoma. Mayo Clin Proc. 2017 Jun;92(6):890–8.*
11. *Neagu TP, Țigliș M, Botezatu D, Enache V, Cobilinschi CO, Vâlcea-Precup MS, et al. Clinical, histological and therapeutic features of Bowen's disease. Romanian J Morphol Embryol Rev Roum Morphol Embryol. 2017;58(1):33–40.*
12. *Parekh V, Seykora JT. Cutaneous Squamous Cell Carcinoma. Clin Lab Med. 2017 Sep;37(3):503–25.*
13. *Henderson SA, Torres-Cabala CA, Curry JL, Bassett RL, Ivan D, Prieto VG, et al. p40 is more specific than p63 for the distinction of atypical fibroxanthoma from other cutaneous spindle cell malignancies. Am J Surg Pathol. 2014 Aug;38(8):1102–10.*
14. *Idriss MH, Barbosa N, Chang MB, Gibson L, Baum CL, Vidal NY. Concomitant hypertrophic lichen planus and squamous cell carcinoma: Clinical features and treatment outcomes. Int J Dermatol. 2022 Dec;61(12):1527–31.*
15. *de Lanna CA, da Silva BNM, de Melo AC, Bonamino MH, Alves LDB, Pinto LFR, et al. Oral Lichen Planus and Oral Squamous Cell Carcinoma share key oncogenic signatures. Sci Rep. 2022 Nov 30;12(1):20645.*
16. *Williams GM, Dreyer MA, Fillman EP. Porokeratosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 2]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK532290/*
17. *Ad Hoc Task Force, Connolly SM, Baker DR, Coldiron BM, Fazio MJ, Storrs PA, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. J Am Acad Dermatol. 2012 Oct;67(4):531–50.*
18. *Chren MM, Linos E, Torres JS, Stuart SE, Parvataneni R, Boscardin WJ. Tumor recurrence 5 years after treatment of cutaneous basal cell carcinoma and squamous cell carcinoma. J Invest Dermatol. 2013 May;133(5):1188–96.*
19. *Mager L, Gardeen S, Carr DR, Shahwan KT. Cemiplimab for the Treatment of Advanced Cutaneous Squamous Cell Carcinoma: Appropriate Patient Selection and Perspectives. Clin Cosmet Investig Dermatol. 2023 Aug;Volume 16:2135–42.*
20. *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 Jul;87(1):131–7.*
21. *Peng L, Wang Y, Hong Y, Ye X, Shi P, Zhang J, et al. Incidence and relative risk of cutaneous squamous cell carcinoma with single-agent BRAF inhibitor and dual BRAF/MEK inhibitors in cancer patients: a meta-analysis. Oncotarget. 2017 Oct 10;8(47):83280–91.*

22. *Mufti A, Sachdeva M, Maliyar K, Sibbald RG. Squamous cell carcinoma arising within discoid lupus erythematous lesions: A systematic review. JAAD Int. 2021 Mar;2:1–4.*
23. *D'Arcy ME, Pfeiffer RM, Rivera DR, Hess GP, Cahoon EK, Arron ST, et al. Voriconazole and the Risk of Keratinocyte Carcinomas Among Lung Transplant Recipients in the United States. JAMA Dermatol. 2020 Jul 1;156(7):772–9.*
24. *Wehner MR, Cidre Serrano W, Nosrati A, Schoen PM, Chren MM, Boscardin J, et al. All-cause mortality in patients with basal and squamous cell carcinoma: A systematic review and meta-analysis. J Am Acad Dermatol. 2018 Apr;78(4):663-672.e3.*
25. *Karia PS, Han J, Schmults CD. Cutaneous squamous cell carcinoma: Estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012. J Am Acad Dermatol. 2013 Jun;68(6):957–66.*

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