Inside The World of Cutaneous Oncology
The UPDATE
Be smart. Protect your skin.

From the Departments of Surgical and Medical Oncology at Providence St. John’s Cancer Institute, we would like to welcome you to the very first edition of The Update, Inside World of Cutaneous Oncology. In this Fall, 2021 issue, we share our insight on the importance of detecting, diagnosing, and managing squamous cell carcinomas. There are multiple clinical trials currently taking place for patients with advanced disease, and we will provide some background and a summary of our trials in this inaugural newsletter.

Our clinical practice focuses on complex oncology with a primary interest in caring for patients with melanoma and other cutaneous (skin) cancers as well as other head and neck diseases. We thank you for taking the time to educate yourself and others about cutaneous cancers.

Skin cancers are the most common cancers worldwide. Both basal cell and squamous cell carcinomas are the most prevalent, with over one million cases expected in the United States in 2021. These numbers are much higher than all other cancers. This past year, many of us were confined to home because of the Covid-19 pandemic.

As the summer is now over and the winter months approach, sometimes we and our patients forget that the UV exposure of the summer months can translate into skin cancers anytime. While we are all generally at risk for cutaneous squamous cell carcinomas, these cancers are, fortunately, rarely deadly.

The diagnosis is made by a skin biopsy and not by exam alone, since squamous cancers and many other skin lesions can look alike. These cancers typically appear as scaling skin that are often the same color as the surrounding skin and are generally found on sun-exposed areas. The risk of these cancers increases with both patient age and level of sun exposure. People who have had one squamous cell carcinoma are at increased risk for additional skin cancers.

Patients with an altered immune system, like organ transplant recipients, are at even higher risk of squamous cell carcinoma. The decision to biopsy a skin lesion is typically made after the assessment by a dermatologist, qualified physician, or advanced practice practitioner (nurse practitioner or physician assistant). The use of confocal microscopy or dermoscopy to increase the accuracy in biopsy is controversial.

The treatment of squamous cell carcinoma
is predominately surgery, although radiation is an option in cases where resection would be disfiguring or the patient doesn’t desire or qualify medically for an operative procedure. Small, localized tumors can be ablated by cryosurgery, laser or intralesional therapies. Removal of the squamous cell carcinoma can involve a simple excision with the conventional approach, which calls for 5 mm margins for low-risk lesions and permanent section analyses.

Most often these procedures are performed under local anesthesia. Larger tumors (> 2 cm in diameter and/or with high-risk features) should be treated with wider margins (6-10 mm). Assessment of the margins is best performed with real-time pathology. Obtaining clear margins is critical to preventing recurrence. Permanent section analyses alone can be performed but may not achieve completely clear edges because of the growth patterns of these cancers is often more extensive than can be seen by the surgeon’s visual inspection and simply measuring margins. Having to perform multiple excisions may not be the best conservative practice.

Moh’s surgery is another method of surgical excision that provides real-time assessment of the tissue edges which helps to reduce the amount of excessive skin removed and improves margin control. This concept is important in cosmetically sensitive areas such as the ear, eye lids, nose, or lips. Moh’s surgery has been demonstrated to have improved primary disease control rates vs conventional excision on the head and neck (there has not been any randomized trials) although both conventional excision and Moh’s have be successful in over 90% of cases. Tissue reconstruction can be performed at the time of excision, or delayed, ensuring that the margins are clear (verified by pathology testing). Radiation therapy has also been shown to be an effective adjuvant treatment for squamous cell carcinomas in patients who are left with positive or close margins or with high-risk tumors: > 2 cm in diameter, depth > 2 mm (or > 6 mm based on the different staging systems), invasion into fat, perineural involvement or poorly differentiated cancers. Both the AJCC and Brigham and Women’s Hospital (BWH) staging systems incorporate these features in their prognosis models.

The risk of occult regional lymph node metastases in cutaneous squamous cell carcinoma can be up to 30% for high-risk lesions. Both the AJCC and BWH staging systems can be used to estimate the risk. Elective lymph node dissection is not recommended, and the role of sentinel node biopsy remains controversial, as the management of occult disease in the lymph nodes can be by surgery, radiation or combination therapy. Patients who develop clinically-evident disease in the regional lymph node basin should have a complete dissection of the affected basin. Radiation to the lymph node basin is generally recommended for patients with multiple tumor-positive lymph nodes and extra-nodal extension.

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recently there was no FDA approved therapy for advanced stage disease. Chemotherapy with a variety of cytotoxic drugs and epidermal growth factor receptor (EGFR) antibodies have modest activity and no cure potential for unresectable SCC.

In 2018, Migden et al published the data from a phase I/II clinical trial for metastatic or locally advanced cutaneous squamous cell carcinomas with the anti-PD-1 antibody cemiplimab demonstrating response rates up to 50%. Since that initial study, two other anti-PD-1 antibodies, nivolumab and pembrolizumab, have shown similar response rates for locally recurrent or metastatic disease.

However, despite these high response rates, disease control rates range from only 50-75% at one year and almost all patients have some toxicity from treatment. There will not likely be any randomized trials for these patients to validate the results, since there is no standard of care to act as the comparator for assessment of response and primary and secondary resistance.

The use of the anti-PD-1 antibodies in immunocompromised individuals, including transplant patients, has not been well studied, and these agents must be used with caution when organ loss could be catastrophic. Patients who are immunosuppressed to prevent graft loss following solid organ transplants are at extremely high risk of SCC and often have aggressive tumors as well as multiple primary SCCs. In addition to effective and safe therapy for recurrent or unresectable disease, finding effective chemoprevention is also a critical unmet need.

We are beginning to better understand the molecular mechanisms of cutaneous squamous cell carcinoma and what makes up the high-risk tumor group; better defining these patients at diagnosis could lead to more effective treatment strategies. Immune checkpoint inhibitors have revolutionized the care of locally recurrent and advanced stage disease, yet not all patients will be cured.

Initiation of immune therapy earlier in the course of disease may be more effective than late treatment—thus, adjuvant systemic immunotherapy is under investigation for patients with resected, high-risk SCC. Other approaches for systemic therapy must be evaluated in the immunocompromised and transplant populations.

Questions? Suggestions, or Contributions?
Please email to: Richard.Essner@providence.org.

For more information or to refer a patient, please call the office at 310.829.8317.
Clinical Trials Summaries:

**Study 1: Fc-Engineered Anti-CTLA-4 Monoclonal Antibody in Advanced Cancer**

A phase I study that study evaluates patients who have failed conventional therapy or no known approved treatment exist and treats patients with modified anti-CTLA-4.

https://www.clinicaltrials.gov/ct2/show/NCT03860272

**Study 2: Intratumoral Cavrotolimod with Pembrolizumab or Cemiplimab in patients with Merkel Cell Carcinoma, Cutaneous Squamous Cell Carcinoma or other advanced solid tumors**

A phase II study of patients with advanced squamous cell carcinoma (or Merkel Cell Carcinoma) to be treated with Pembrolizumab or Cavrotolimod in combination with intra-tumoral Cavrotolimod (a toll-like receptor 9 agonist assigned to activate innate immunity).

https://www.clinicaltrials.gov/ct2/show/NCT03684785?term=exicure&draw=2&rank=1#contacts

**Study 3: (Co8 PET TRACER) for Positron Tomography (PT/CT) in patients with metastatic solid tumors**

A phase II study, open label multidose study of 89Zr-Dr-IAB22MC (Co8 PET TRACER) for Positron Tomography (PT/CT) in patients with advanced cancers receiving standard of care immunotherapy. The goal of the study is to use immune cell monitoring (CD8 labeled cells) to determine the efficacy of immunotherapy.

https://www.clinicaltrials.gov/ct2/show/NCT03802123?term=ImaginAb&draw=2&rank=1

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