NCCN GUIDELINES FOR PATIENTS®

2023

# Squamous Cell Skin Cancer



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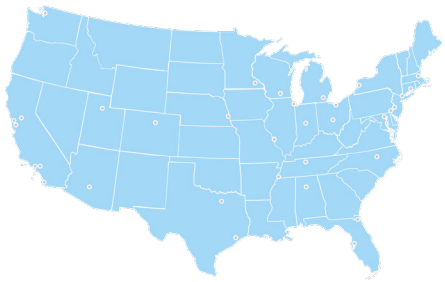
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National Comprehensive Cancer Network®



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Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

**These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Squamous Cell Skin Cancer, Version 1.2023 – March 10, 2023.**

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# 1
# Squamous cell skin cancer basics


5 Skin basics

6 Risk factors

8 Diagnosis

11 Key points

**Squamous cell skin cancer is the second most common type of skin cancer. It is highly treatable and can often be cured.**

Squamous cell skin cancer is a common skin cancer, especially in fair-skinned people. It is the second most common type of skin cancer, after basal cell carcinoma. The third type—melanoma—is much less common than the other types but can be more aggressive. Because they do not behave like melanoma, basal cell and squamous cell skin cancers are often referred to as nonmelanoma skin cancers or keratinocyte carcinomas.

Cancer that starts in a squamous cell is called a squamous cell carcinoma. Squamous cells are found in the top layer of the skin. They can also be found in other areas of the body, such as the lungs, thyroid, and esophagus. These types are treated differently than cutaneous squamous cell carcinoma.

Squamous cell skin cancers often begin as scaly patches on the skin that can become solid and misshapen. This cancer is also called cutaneous squamous cell carcinoma (CSCC). This patient guide is about squamous cell skin cancer only. The terms “squamous cell skin cancer” and “CSCC” are used interchangeably throughout this guide.

## Skin basics

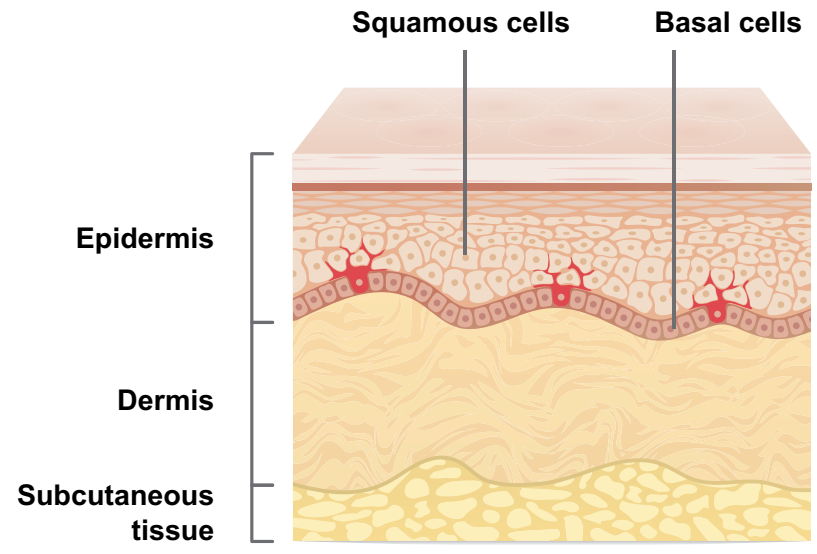
Your skin is the largest organ of the body. Skin protects you from invaders (such as microbes), helps control body temperature, and allows the sensations of touch, heat, and cold.

Skin has 3 layers:

- **Epidermis** is the outermost (top) layer of skin that provides a waterproof barrier and creates skin color (melanin).
- **Dermis** contains connective tissue, hair follicles, and sweat glands.
- **Hypodermis (subcutis)** is the deepest layer, made up of fat and connective tissue.

**Layers and cell structure of skin**

**Squamous cells are found in the top layer of skin, called the epidermis.**



Skin cancers are often formed in the epidermis. There are 3 main types of cells in the epidermis:

- **Squamous cells:** These cells are thin, flat cells that look like fish scales, and are found in the tissue that forms the surface of the skin.
- **Basal cells:** These cells are found in the lower part of the epidermis, called the basal cell layer. Basal cells constantly divide to form new cells to replace the squamous cells that wear off of the skin's surface. As these cells move up in the epidermis, they get flatter, eventually becoming squamous cells.
- **Melanocytes:** These cells are found in the top layer of skin. Melanin is produced in the melanocytes. Melanin is responsible for the color of our hair, skin, and eyes. In addition to providing color, melanin also protects our skin from harmful ultraviolet (UV) rays.

# Risk factors

A risk factor is something that increases the chances of getting a disease. For example, smoking cigarettes is a risk factor for developing lung cancer. The major risk factors for squamous cell skin cancer are described next.

## Sunlight/outdoor tanning

Most squamous cell skin cancers are caused by spending too much time in the sun over the course of many years, especially in people who sunburn easily. People with light skin, hair, and eyes who have been in the sun very often throughout their lives are at the highest risk for squamous cell skin cancer. People who work outdoors are also at higher risk. Because long-term sun exposure can lead to squamous cell skin cancer, it is more common in people who have spent more years in the sun.

### Sun exposure

**Most squamous cell skin cancers are caused by spending too much time in the sun over a long period of time, frequent tanning, and getting sunburns.**



## Indoor tanning

Indoor tanning is a major risk factor for squamous cell skin cancer. Using all types of indoor tanning machines (eg, booths, beds) increases the risk of getting any type of skin cancer.

## Environmental toxins

People who are often exposed to pollutants such as tobacco smoke, exhaust from cars or other vehicles, and arsenic (which can be found in soil, water, and air) can experience skin damage that can lead to squamous cell carcinoma.

## Scars and chronic wounds

CSCC can form in scars or chronic (non-healing) wounds, such as ulcers (sores) and burns. This is known as Marjolin's ulcer. CSCC that starts in damaged, inflamed, or scarred skin is difficult to treat and more likely to come back after treatment.

## Actinic keratoses

An actinic keratosis is an area of scaly or rough skin caused by exposure to the sun over time that may become squamous cell skin cancer. Actinic keratoses vary in appearance, and may be red, white, tan, or pink in color. They may appear as small scaly spots (lesions) or stick out from the skin like bumps. Some may even look like warts.

Having actinic keratoses means you are at increased risk of developing squamous cell skin cancer. It is important that you have your skin looked at by a doctor or dermatologist.

### Actinic keratosis on the hand

**An actinic keratosis is an area of rough skin caused by being in the sun over time.**



### Actinic keratosis on top of head

**Actinic keratoses can vary in appearance and may be red, white, tan, or pink in color.**



### Genetic syndromes

Having certain genetic syndromes means you are at higher risk of getting squamous cell skin cancer. While there are many, these syndromes include:

- Xeroderma pigmentosum (XP), a condition in which the body isn't able to repair damage to DNA caused by sunlight. Skin cells with a lot of DNA damage can eventually become skin cancers.
- Recessive dystrophic epidermolysis bullosa (RDEB), a form of a rare, inherited skin disorder that causes the skin to become very fragile. Any trauma to the skin can cause painful blisters.

NCCN recommends that people with these or other genetic syndromes should be referred to a cancer center with expertise in CSCC prevention and treatment.

NCCN also recommends that those with a genetic risk of skin cancer receive counseling from someone with expertise in cancer genetics throughout the treatment process. This might be a genetic counselor, medical geneticist, endocrinologist, oncologist, surgeon, or an oncology nurse.

### Weakened immune system

When your immune system is weakened, your body has trouble fighting off viruses, bacteria, and fungi. This can lead to infections and other health risks. Having a weakened immune system can put you at risk of squamous cell skin cancer. An example of when this happens is after organ transplantation. If you received an organ from another person, you likely take drugs to stop your body from attacking the donated organ. These drugs, called immunosuppressants, also reduce the body's ability to fight infection and disease.

The immune system also may not work well if you have other health conditions, such as:

- Lymphoma (cancer of the lymph nodes)
- Chronic lymphocytic leukemia (cancer of white blood cells in bone marrow)
- Human immunodeficiency virus (HIV) or AIDS

Any of these conditions can weaken the immune system, which can increase the risk of getting squamous cell skin cancer. Everyone with this condition should undergo skin cancer screening on a regular basis.

## Diagnosis

If you have an area of abnormal-looking skin (called a lesion) that looks like it could be skin cancer, the next step is testing. This will likely include:

- A full health history
- A close examination of the lesion(s)
- A skin biopsy to remove a sample of the lesion and test it for cancer (this is the only way to know for sure if there's cancer)
- Imaging scans if cancer may be deep within the skin or spread to other parts of the body

### Biopsy

If a concerning lesion is found on your skin, some or all of it will be removed and sent to a lab to be looked at under a microscope. This is called a skin biopsy. A biopsy is needed to

diagnose squamous cell skin cancer. Your sample should be reviewed by a pathologist. The pathologist will note the overall appearance and the size, shape, and type of your cells.

There are several ways to do a skin biopsy. Your doctor will choose one based on the size of the affected area, where it is on your body, and other factors. Any biopsy is likely to leave at least a small scar. Different methods can result in different types of scars. Talk to your doctor about the type of biopsy and the risk of scarring before you have the biopsy.

No matter which type of biopsy is done, it should remove as much of the suspected area as possible for an accurate diagnosis to be made.

Skin biopsies are done using a local anesthetic (numbing medicine), which is injected into the area with a very small needle. You will likely feel a small prick and a little stinging as the medicine is injected, but you should not feel any pain during the biopsy.

### Skin shave biopsy

A skin shave biopsy can be done on the skin surface (superficial) or deeper. Superficial shave biopsies are useful for very flat skin lesions. This type of biopsy removes the top layer of skin (epidermis) and part of the dermis using a tool similar to a razor.

### Skin punch biopsy

During a skin punch biopsy, a small piece of skin and connective tissue are removed using a hand-held tool. Stitches are often used to close the opening in the skin.

### Excision biopsy

During an excision biopsy, all or part of the lesion is removed. This biopsy can be done in a doctor's office or at a hospital. You may want to ask how the biopsy incision will be closed, as there are several options that can be used.



## Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- ✓ Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- ✓ Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- ✓ Create folders for insurance forms, test types (blood, imaging, pathology, radiology, and genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

## Imaging tests

Your doctor may use imaging scans to see if you have cancer beyond the suspicious-looking lesion, such as in the bone, nerves, or surrounding deep soft tissue. You may have a computed tomography (CT) scan or an MRI.

A CT scan is a procedure that uses a computer linked to an x-ray machine to make detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional (3-D) views of tissues and organs.

An MRI is a procedure that uses radio waves, a powerful magnet, and a computer to make detailed pictures of areas inside the body.

For both a CT scan and an MRI, a liquid called a contrast dye may be injected into a vein to help your tissues and organs show up more clearly in the picture. Using a contrast dye for both the CT scan and the MRI is preferred unless it is contraindicated, which means you have an allergy or condition that could result in a harmful reaction.

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is injected into a vein (through an IV using a needle). The needle is most often inserted on the inside of your elbow.

The tracer travels through your blood and collects in organs and tissues. This helps the radiologist see certain areas more clearly. You may need to wait for the tracer to be absorbed by your body, which takes about 1 hour.

The tracer is attached to a substance that your cells and tissues use. Cancer cells use the substance differently than non-cancer cells. The radioactive part of the tracer lets your care team see how your cells are using the substance. This helps them find any usage that is not normal.

Cancer cells show up as bright spots on PET scans. Not all bright spots are cancer. When a PET scan is combined with CT, it is called a PET/CT scan.

### Cutaneous squamous cell carcinoma (CSCC)

- ✓ A very common type of skin cancer
- ✓ Occurs more often in lighter-skinned people
- ✓ Is commonly found in areas of the body exposed to sun, especially the head and neck
- ✓ Rarely spreads to distant areas of the body
- ✓ Can spread in the area where it first forms
- ✓ If not treated can cause severe skin damage and even death
- ✓ Most people (over 95%) can be cured by completely removing the CSCC

## Confirmed CSCC

Once a diagnosis of CSCC is made, your doctor will follow up with:

- A complete head-to-toe skin exam to look for other lesions
- An exam of the lymph nodes

Cancer cells can travel through blood and a fluid called lymph to form tumors in other parts of the body. Lymph nodes are small, bean-shaped structures that are part of the body's immune system. Lymph nodes filter substances that travel through the lymphatic fluid. They contain lymphocytes (white blood cells) that help the body fight infection and disease.

If your lymph nodes feel larger than they should be, cancer may have spread to the lymph nodes (this is also called “nodal disease”). To find out, your doctor will use a needle biopsy to take a sample from the lymph node for testing.

Squamous cell skin cancer that has not spread to nearby lymph nodes is referred to as “local” squamous cell skin cancer.

➲ *See Part 3 for more information on local CSCC.*

If cancer is found in the lymph nodes, it is called “regional” squamous cell skin cancer.

➲ *See Part 4 for more information on regional CSCC.*

“

Knowing there is treatment available gave me hope at diagnosis and for the future. "

## Key points

- Squamous cell skin cancer is the second most common type of skin cancer. It is highly treatable and can often be cured.
- Squamous cell skin cancer is most commonly caused by getting sunburns or spending too much time in the sun over many years.
- An actinic keratosis is an area of scaly or rough skin that has a higher chance of becoming squamous cell skin cancer.
- You may be more likely to get squamous cell skin cancer if you have actinic keratoses, a weakened immune system, or certain genetic syndromes.
- Squamous cell skin cancer can form in old wounds, burns, or scars. This is called Marjolin’s ulcer and it can be harder to treat.
- Testing for CSCC could include a full health history, an examination of any lesions, and a skin biopsy to remove a sample and test it for cancer.
- Imaging scans will also be done if cancer goes deeper into the skin or has spread to other parts of the body.
- Cancer cells can travel through blood and lymph fluid to form tumors in other parts of the body. If spread to lymph nodes is suspected, your doctor will do a lymph node biopsy.

# 2
# Types of treatments


13 Who is on my care team?

14 Superficial treatments

16 Surgery

19 Radiation therapy

20 Systemic therapy

22 Clinical trials

23 Key points

**This chapter describes the types of treatment you may have for squamous cell skin cancer. The best treatment for you will depend on the extent of the cancer, whether surgery is a suitable option, and your personal preferences. Not everyone will receive the same treatment.**

## Who is on my care team?

After being diagnosed with squamous cell skin cancer, knowing what to do next can be confusing. Aside from your oncologist (your cancer doctor), there are others who may be involved in your cancer care.

Some members of your care team will be with you throughout your treatment, while others will only be there for parts of it. Get to know your care team and let them get to know you.

Depending on your diagnosis, your care team might include the following:

**Dermatologists** are doctors who diagnose and treat skin conditions, including skin cancer. They also do skin exams and can teach you how to do them on your own.

**Mohs surgeons** are doctors (usually dermatologists) who have advanced training in Mohs surgery and reconstruction after surgery. They remove the tumor, ensure no more cancer can be seen using a microscope, and can restore the appearance of the affected area with reconstructive surgery.

**Surgical oncologists** are doctors who are trained to diagnose and surgically treat and remove cancerous tumors, including those that have spread beyond the skin.

**Medical oncologists** are doctors who specialize in prescribing cancer-treatment drugs (chemotherapy). They are trained to diagnose and treat cancer using medicines that may be taken by mouth, be injected, or be given intravenously (through a vein).

**Pathologists** are doctors who are trained to study tissue and cells removed during a biopsy under a microscope to determine the stage of a cancerous tumor.

**Plastic surgeons** are doctors who can remove cancer as well as reconstruct, restore, and repair body parts. They may work with a pathologist at the time of your surgery for more immediate results. They are trained to close a wound after surgery, especially if it involves deeper tissue where general anesthesia may be needed.

**Head and neck surgeons** are doctors who are trained to treat conditions (cancerous and noncancerous) of the deeper parts of the head and neck, including the ears, nose, and throat.

**Radiation oncologists** are doctors who are trained to use different types of radiation therapy.

**Pharmacists** are medical professionals who are trained to prepare and give out medicine and explain their proper use and any side effects. Some pharmacists specifically work with people with cancer.

**Geneticists** are doctors who study how traits are passed down from parents to children through genes. They are trained to diagnose and treat genetic disorders and counsel people and families at risk.

**Oncology nurses** are nurses who provide hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects. Sometimes, these experts are called **nurse navigators**.

You know your body better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not
- Your goals for treatment

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

# Superficial treatments

Treatments that affect only the top layer of the skin are called superficial treatments. They may be used to treat the earliest form of squamous cell skin cancer, called Bowen's disease. They are also used for actinic keratoses (pre-cancerous lesions) that are in the same general area as the Bowen's lesion.

## Photodynamic therapy

In photodynamic therapy (PDT), a light-sensitive drug is applied to the area. When exposed to light (either red or blue light in the doctor's office, or shaded outdoor light), the drug becomes active and kills cancer cells.

Common side effects of PDT include itching or burning when the liquid is applied, pain during the red or blue light exposure, and itching and redness for a few days after treatment.

**Photodynamic therapy**

**A drug applied to the skin becomes active and kills cancer cells when exposed to light.**



## Cryotherapy

Cryotherapy (also called cryosurgery) freezes and destroys precancerous and cancerous cells using a very cold liquid or tool. Liquid nitrogen is often used. Cryotherapy sometimes causes a burning sensation during treatment. A blister and scab will form, which heals over 2 to 3 weeks. Skin darkening or lightening can happen while it is healing.

## Topical therapies

Topical therapies are treatments that are applied to the skin.

5-fluorouracil (Carac, Efudex, Fluoroplex) and imiquimod (Aldara) are prescription creams used to treat early CSCC and actinic keratoses. 5-fluorouracil (also called 5-FU) is chemotherapy applied directly to the skin, unlike most chemotherapy that is put into the bloodstream.

A cream called calcipotriene (Sorilux, Dovonex) is often used with 5-fluorouracil to treat actinic keratosis. Calcipotriene is a form of vitamin D that activates the skin's immune system.

Imiquimod belongs to a group of drugs known as immune response modifiers. This cream can help fight abnormal skin growths by activating the immune system to damage abnormal skin cells.

Tirbanibulin (Klisyri) is another topical therapy used to treat actinic keratosis. Tirbanibulin is a type of medication called a microtubule inhibitor. It works by killing fast-growing cells, such as the abnormal cells that cause actinic keratoses. It is applied to the face or scalp 1 time a day for 5 days in a row (consecutive) using a single-dose packet with each application.

Thickening of the outer layer of skin is known as hyperkeratosis. The goal is to soften and break down this thick top layer before treatment. For hyperkeratotic (thick and rough) actinic keratoses, one or more of the following may be used before treatment with the therapies described above.

**Cryotherapy**

**Cryotherapy freezes and destroys cancer cells using a very cold liquid or tool.**



- Topical tazarotene (a retinoid product related to vitamin A)
- Curettage (scraping away skin with a spoon-shaped tool)
- Topical keratolytics (also called topical urea, lactic acid, or salicylic acid)

Other therapies that are sometimes used for actinic keratoses include topical diclofenac, chemical peels (trichloroacetic acid), and resurfacing techniques such as laser or dermabrasion.

Topical therapies for squamous cell skin cancer may cause burning, redness, itching, and pain in the treated area. Sun-damaged skin may also need to be re-treated with topical therapies from time to time.

# Surgery

Different types of surgery can be used to treat squamous cell skin cancers. Most surgery procedures involve a form of excision, which means cutting out the tumor along with a small margin of normal skin.

## Curettage and electrodesiccation (C&E)

C&E is done in a medical office with local numbing to the area. In this method, the visible tumor is first scraped off using a thin tool with a sharp loop or spoon at the end. Next, an electric needle is used to cauterize (burn) the base of the wound. This usually kills any remaining cancer cells and helps stop bleeding. This two-step system of scraping then burning may be done up to three times in the same session. C&E is a recommended option for early CSCC on the surface of the skin that has not spread to lymph nodes.

## PDEMA/Mohs surgery

Peripheral and deep en face margin assessment (PDEMA) is a type of surgery often used for treatment on the head, face, hands, feet, shins, and genital areas, because it can remove the cancer while sparing as

**Mohs surgery**

**This procedure allows the surgeon to know right away whether all cancer was removed.**



much normal tissue as possible. It should be performed by surgeons who have special training and experience in this procedure.

All forms of PDEMA allow for complete testing of the edges of any removed tissue.

Mohs surgery is the most common form of PDEMA. Mohs surgery can be done in a medical office or surgical suite and should be done by a dermatologic (skin) surgeon who has special training and experience in this procedure. Most patients remain awake during the procedure. After the area is numbed, the visible tumor is first removed using a scalpel. Next, a thin layer of surrounding tissue is removed from under and around the wound. The edges and underside of this tissue are evaluated by the Mohs surgeon using a microscope while you wait.

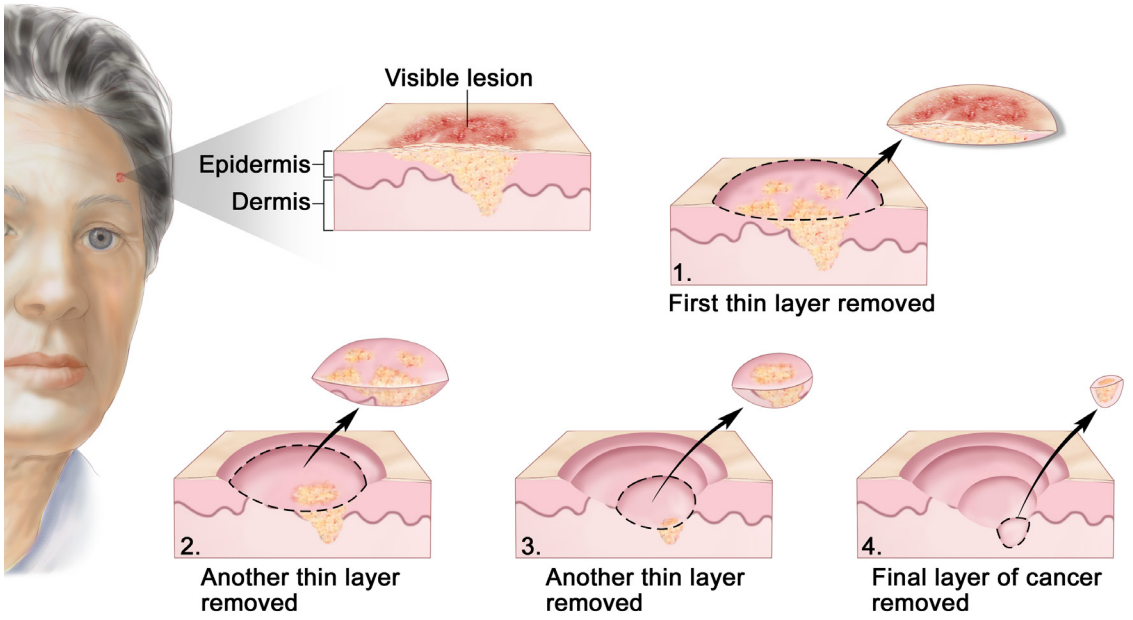
If cancer cells are seen by the surgeon, another thin layer of tissue is removed only from the area of the wound where the cancer was seen. When a removed layer shows no cancer cells at its edges, the procedure is over.

## Standard surgical excision

Standard surgical excision is another option for treating squamous cell skin cancer. A standard surgical excision (removal) can be done in a medical office while you are awake. After the area is numbed, the doctor removes the tumor and an area of normal tissue surrounding it with a scalpel blade. The edges of the removed tissue are called the surgical margin. PDEMA can also be used with standard surgical excision. The tissue is then sent for testing. A pathologist examines thin samples of

### Mohs surgery

**Mohs surgery is a recommended option for CSCC that has not spread to lymph nodes and is preferred for very high-risk local CSCC.**




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the tissue under a microscope to see if there are cancer cells at the margin.

## Lymph node dissection

If lymph nodes near a squamous cell skin cancer tumor are enlarged, the doctor might biopsy them to check for cancer cells.

If the lymph node biopsy shows cancer, sometimes many nodes might be removed in a more extensive surgery called a lymph node dissection. The nodes are then looked at under a microscope for signs of cancer. This type of surgery is more extensive than surgery on the skin and is usually done while you are under general anesthesia (in a deep sleep).

## Sentinel lymph node biopsy

A sentinel lymph node is the first lymph node to which cancer cells most likely spread from a primary tumor. Sometimes, there is more than one sentinel lymph node.

A sentinel lymph node biopsy (SLNB) is a surgery that removes tissue samples to examine sentinel nodes. The lymph nodes will be checked for cancer cells by a pathologist in a lab. Sometimes people can have an SLNB at the same time as surgery. The results will be used to stage the cancer and plan treatment.

To locate the sentinel lymph node(s), your surgeon will inject a radioactive, blue-colored substance into your skin near the tumor. The substance will drain into the sentinel lymph nodes. Your surgeon will identify the sentinel lymph nodes using a device and remove them through a small cut in your skin. This procedure is generally done under general anesthesia.

## Wound healing after surgery

After surgery, there are different ways a wound can heal.

Some wounds heal better without stitches. A wound might be left open (rather than being stitched together) and left to heal by itself, filling in and closing up naturally. This is called **secondary intention healing**. It could mean you will need regular dressings to the area for up to 6 weeks, but the full time to heal depends on the size, depth, and area of the wound.

A **linear closure** is another common form of wound healing. The surgeon will cut a small amount of extra skin to change the shape of the wound from a circle to a fusiform (an oval that looks like a football) to help the surgeon stitch the wound together in a line.

Other wounds may need **skin grafts** or other types of surgery (such as rearranging skin, known as “flapping”) to heal well and lessen scarring. A skin graft is a patch of skin that is removed by surgery from one area of the body and transplanted (attached) to another area. This may be done the same day or a few days after a PDEMA/Mohs procedure or standard surgical excision.

After surgery, your skin will continue healing for a period of between 6 to 10 weeks. Scar treatment and aftercare for the skin around the wound will likely be recommended.

# Radiation therapy

Radiation therapy (RT) is a type of cancer treatment that uses beams of intense energy – from electrons (beams), photons (high-energy x-rays), or protons (charged particles) -- to kill cancer cells. Radiation therapy usually involves 5 daily brief treatments per week over 3 to 7 weeks. Radiation treatments should be given by a practicing radiation oncologist (a doctor who is an expert in radiation treatment).

## Types of radiation therapy

There are two general types of radiation therapy that can be used to treat CSCC: external beam radiation therapy (EBRT) and brachytherapy.

In EBRT, a beam of radiation is directed at the tumor from a machine. The two most common types of external beam radiation for CSCC are electrons and photons. Electrons are used to treat superficial tumors. Photons are used to treat deeper, more invasive tumors.

In brachytherapy, a radiation source is placed close to or in direct contact with the tumor for a short period of time.

## Uses for radiation therapy

Radiation therapy is an option for people after resection (surgery) of their cancer, or for those who cannot or choose not to have surgery. However, radiation therapy can be very effective for small tumors, and for tumors in areas such as the head and neck.

Radiation therapy should not be used in people who have certain genetic conditions that put them at higher risk of skin cancer caused by radiation, such as basal cell nevus syndrome or xeroderma pigmentosum. It may also not be appropriate for some people who have connective tissue diseases, such as lupus or scleroderma.

The same area generally should not be treated with radiation more than once. When CSCC grows in a radiated area, it usually needs to be removed with surgery. However, the area often doesn't heal as well because the tissues were weakened by the radiation. This is especially true for CSCC on the scalp.

A radiation oncologist should help you determine whether this treatment is appropriate for you.

Adjuvant therapy refers to therapy that is given after primary treatment to lower the risk that cancer will come back. Radiation is sometimes used as adjuvant therapy after surgery to kill any remaining cancer cells, or to help prevent recurrence for patients with high-risk tumors.

## Side effects of radiation therapy

The most common short-term side effects of radiation are skin redness, itching, mild discomfort, and feeling tired. These side effects are worse at the end of the radiation course and take several weeks to go away.

Potential long-term side effects of radiation include hardening of the skin and soft tissue in the treatment area, mild change in skin color (lightening or darkening), and spider veins. More serious long-term side effects include non-healing ulcers and cataracts (for CSCC in the eye area). If you are treated with radiation, you could develop a second cancer in the treated area, but this is rare. This is more common in young patients many years (decades) later.

# Systemic therapy

Systemic therapy is treatment with medicine(s) that travel in the bloodstream to reach cells throughout the body. Systemic therapies can affect both cancer cells and normal cells, and they can have side effects. They are given intravenously (through the veins) or taken by mouth as a pill. Categories of systemic therapy are described below.

## Chemotherapy

Chemotherapy uses drugs to kill fast-growing cancer cells. Some chemotherapy medicines contain the metal platinum. Cisplatin and carboplatin are platinum chemotherapies used to treat squamous cell skin cancer and other cancers. They may be given in combination with other chemotherapy drugs.

## Targeted therapy

Targeted therapies are medicines that can target and attack specific types of receptors on cancer cells. The targeted therapies used to treat squamous cell skin cancer are known as epidermal growth factor receptor (EGFR) inhibitors. EGFR is a protein found on the surface of cells that causes them to divide. Inhibiting (blocking) EGFR may keep cancer cells from growing. Cetuximab (Erbitux) is an EGFR inhibitor used to treat CSCC and other cancers.

## Immunotherapy

Immunotherapy stimulates the activity of the immune system, which can improve the body's ability to find and destroy cancer cells. Immunotherapies used to treat CSCC and other cancers are known as programmed death ligand 1 (PD-1) inhibitors. PD-1 inhibitors are a type of immune checkpoint inhibitor. Cemiplimab (Libtayo) and pembrolizumab (Keytruda) are PD-1 inhibitors used to treat squamous cell skin cancer and other cancers.

## Uses for systemic therapy

Systemic therapy is not often used by itself to treat squamous cell skin cancer. It may be used in combination with radiation therapy to treat CSCC that can't be removed using surgery.

Systemic therapy alone may also be an option if both surgery and radiation therapy are not possible or were not successful. In this case, immunotherapy with a PD-1 inhibitor is preferred.

## Side effects of systemic therapy

If you are prescribed systemic therapy, you may experience side effects. The side effects of systemic therapy vary greatly depending on the medicine(s) used. Most side effects start when treatment starts and stop when it's over, but some can occur months or even years later. Common side effects include:

- Tiredness and muscle fatigue
- Nausea/vomiting
- Loss of appetite
- Head and body aches
- Diarrhea or constipation

More severe side effects include lung and breathing problems, damage to organs, high blood pressure, or abnormal bleeding. Longer-term side effects of systemic therapy can include other cancers, heart disease, and infertility.

## Side effects of systemic therapy

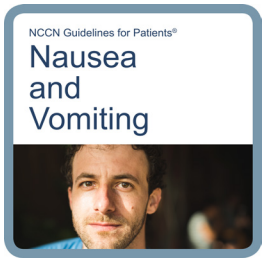
If you are prescribed systemic therapy, you may experience some side effects. They include:

- ✓ Tiredness (fatigue)
- ✓ Nausea and vomiting
- ✓ Lung and breathing problems (eg, cough, shortness of breath, chest pain)
- ✓ Damage to major organs including the liver and kidneys
- ✓ Hair loss
- ✓ Mouth sores
- ✓ Body aches
- ✓ Rashes and other skin problems
- ✓ Loss of appetite
- ✓ Diarrhea
- ✓ Constipation
- ✓ Low blood cell counts
- ✓ High blood pressure
- ✓ Abnormal bleeding
- ✓ Side effects of immunotherapy known as immune-related adverse events (irAEs)

Not all side effects are listed here. You can ask your care team for a more complete list and discuss any concerns you might have.

More information on the side effects of immune checkpoint inhibitors and on managing nausea following treatment is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



# Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

## Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase 1** trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the long-term safety and benefit of an FDA-approved treatment.

## Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

## Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

## Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

## Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

### Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.



## Finding a clinical trial

### In the United States

**NCCN Cancer Centers**
NCCN.org/cancercenters

**The National Cancer Institute (NCI)**
cancer.gov/about-cancer/treatment/clinical-trials/search

### Worldwide

**The U.S. National Library of Medicine (NLM)**
clinicaltrials.gov/

### Need help finding a clinical trial?

**NCI's Cancer Information Service (CIS)**
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

**Are clinical trials free?**
There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care.

This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

## Key points

- Photodynamic therapy, cryotherapy, and topical therapy are treatment options for actinic keratoses (pre-cancerous lesions).
- Types of surgery for squamous cell skin cancer include curettage and electrodesiccation, PDEMA/Mohs surgery, and standard surgical excision.
- Radiation therapy is a treatment option for people who cannot or choose not to have surgery. For the treatment of some squamous cell skin cancers, it is used after surgery to kill remaining cancer cells.
- Systemic therapy (eg, chemotherapy, targeted therapy, immunotherapy) is not used often for CSCC, except when it has spread elsewhere in the body. It may be an option if surgery and radiation therapy are not possible or were not successful.
- Enrolling in a clinical trial is another option for treatment. Talk with your care team about seeing if you qualify for a clinical trial if one is available.

# 3

# Local cutaneous squamous cell carcinoma (CSCC)


25 Risk assessment

27 Low-risk

28 High-risk or very high-risk

29 Key points

**Squamous cell skin cancer that has not spread to nearby lymph nodes is known as "local". Local disease is usually treated with surgery. The goal of treatment is to remove all of the cancer with as little damage to the surrounding skin as possible.**

# Risk assessment

After squamous cell skin cancer is confirmed, your doctor will consider several features of the cancer to determine if it is a low-, high-, or very high-risk skin cancer. This is important to know because high- or very high-risk disease is treated differently than low-risk disease. A high-risk CSCC has an increased risk of local recurrence. A very high-risk CSCC has an increased risk of local recurrence and of metastasis (spread).

The risk level or category for skin cancer is usually based on the highest risk factor found. The following factors are used to determine your risk level.

## Location and size

Squamous cell skin cancer on the head or neck is more likely to return after treatment than tumors on the trunk, arms, or legs. The following tumors are considered high risk because of their location and/or size:

- Tumors on the trunk, arms, or legs that are between 2 centimeters (cm) (about the size of a nickel) and 4 cm (about the size of a quarter)
- Any size tumor on the head, face, neck, hands, feet, shins, or sex organs

The following tumors are considered very high risk because of their size:

- Any tumor over 4 cm in any location

### Get to know your care team

**Keep the names and contact information for each member of your care team on hand, so you know whom to contact with questions or concerns.**



## Tumor shape

If the clinical extent (border) of the tumor is well-defined, it is considered low risk. If the border isn't well-defined and has an uneven shape, it is considered high risk.

## Tumor return after treatment

Recurrent tumors are cancer that has returned after treatment, usually after a period of time during which the cancer could not be detected. All treatment types have a risk of recurrence. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Any tumor that has returned after treatment is considered a high-risk squamous cell skin cancer.

## Tumor formed in damaged skin

If squamous cell skin cancer starts in an area that was previously treated with radiation therapy, it is considered a high-risk cancer. This is also the case if the cancer starts in a wound, a scar, or an area of damaged or inflamed skin.

## Nerve damage

If the tumor has grown into a nerve or group of nerves, usually seen under a microscope, it is considered a high-risk or very high-risk cancer. This is also called perineural invasion. Signs that the cancer may have invaded nerves include pain, burning, stinging, loss of feeling or movement, and double or blurred vision.

## Tumor grade

The tumor grade is a rating of how fast your doctors expect the cancer to grow and spread. It is based on how different the tumor cells look compared to normal cells under a microscope. The more different they look, the higher the risk of spreading.

## Tumor type

To diagnose squamous cell skin cancer, you likely had a small sample of tissue removed for testing (a skin biopsy). That tissue sample was then analyzed by a pathologist in order to determine the specific type (and subtype) of cancer. There are certain rare subtypes of squamous cell skin cancer that are more likely to return after treatment.

## Connective tissue in the tumor

Some tumors form fibrous or connective tissue, which is a sign of a high-risk or very high-risk cancer.

## How deep the tumor is

The deeper the tumor has invaded into the skin, the higher the risk of the cancer returning after treatment or spreading to distant sites.

## Cancer cells in lymph or blood vessels

If there are cancer cells in the blood vessels or lymph vessels outside of the main tumor, it means that the cancer is more likely to spread to nearby lymph nodes and other parts of the body. This is known as lymphovascular invasion.

## Weakened immune system

People with a weakened immune system have a higher risk of getting CSCC, and they are at higher risk of cancer returning after treatment. Examples of conditions that weaken the immune system include long-term corticosteroid use, having human immunodeficiency virus (HIV) or AIDS, or having received an organ transplant.

# Low-risk

Surgery is the preferred treatment for low-risk CSCC that has not spread to lymph nodes. The options for surgery include:

- Curettage and electrodesiccation (C&E) or shave excision
- Standard surgical excision
- Mohs surgery or another form of PDEMA

If you are not a candidate for surgery, treatment with radiation therapy is recommended if you can have it.

## Curettage and electrodesiccation

C&E or shave excision are recommended treatment options for low-risk, local CSCC. Usually it is considered for early, small CSCC on the surface of the skin. If the tumor ends up being deeper than expected into the skin during the procedure, a standard surgical or shave excision should be performed rather than C&E to remove deep areas of cancerous tissue.

## Standard surgical excision

Standard surgical excision is a recommended treatment option for low-risk, local CSCC. If testing after surgery finds cancer cells in the surrounding tissue removed with the tumor, more treatment is needed. Further treatment options include:

- Mohs surgery or resection with PDEMA
- Another surgical excision
- Radiation therapy (if more surgery cannot be done)

## Mohs surgery or PDEMA

Mohs surgery or another form of PDEMA is a recommended treatment option for low-risk CSCC that has not spread to lymph nodes.

➲ *See Part 2: Types of treatment for more detailed descriptions of these treatments.*

### If you smoke or vape, seek help to quit

If you smoke tobacco or use e-cigarettes, it is very important to quit. Smoking can limit how well cancer treatment works. Smoking greatly increases your chances of having side effects during and after surgery. It also increases your chances of developing other cancers.

Nicotine is the chemical in tobacco that makes you want to keep smoking. Nicotine withdrawal is challenging for most smokers. The stress of having cancer may make it even harder to quit. If you smoke, ask your doctor about counseling and medicines that can help you quit.

For online support, try these websites:

- SmokeFree.gov
- BeTobaccoFree.gov
- CDC.gov/tobacco

# High-risk or very high-risk

Surgery is the preferred treatment for high-risk or very high-risk CSCC that has not spread to lymph nodes. The options for surgery include:

- Mohs surgery or another form of PDEMA (preferred for very high-risk CSCC)
- Standard surgical excision

If you are not a candidate for surgery, see **If surgery is not an option** on the next page.

## Mohs surgery or another form of PDEMA

Mohs surgery or another form of PDEMA is the preferred treatment option for very high-risk cancer that has not spread to lymph nodes. Before or during PDEMA, your doctor may consider a sentinel lymph node biopsy (SLNB). An SLNB is used to identify the first lymph nodes where cancer might have spread. The surgeon uses a harmless dye and a low-level radioactive solution to find the sentinel nodes. The nodes are then removed and tested for signs of cancer.

If Mohs surgery or another form of PDEMA removes the cancer, but other concerning features are noted during surgery, a discussion with different cancer doctors is recommended to determine next steps. Treatment with radiation therapy will be considered.

If Mohs surgery or another form of PDEMA does not remove all of the cancer, a discussion between different cancer doctors is recommended to consider next treatment options. If another surgery can be performed, this is often tried first. Otherwise, radiation therapy is recommended. In some cases, systemic therapy is used in addition to radiation. Platinum-based chemotherapy is a recommended option for use with radiation if you can have it. Enrolling in a clinical trial for systemic therapy may also be an option.

If radiation therapy is not expected to kill the cancer completely or may damage critical healthy organs, systemic therapy alone is recommended. If you are eligible, immunotherapy with an immune checkpoint inhibitor is preferred.

## Standard surgical excision

Standard surgical excision is a recommended treatment option for high-risk or very high-risk local CSCC. A wider margin (area of normal tissue around the lesion) is removed for high-risk or very high-risk CSCC.

If standard surgical excision is successful at removing the cancer but other concerning features are noted during surgery, a discussion with different cancer doctors is recommended to determine next steps. Treatment with radiation therapy will be considered.

If testing after surgery finds cancer in the margin, more treatment is needed. If Mohs surgery or another form of PDEMA is possible, it is usually tried first. Otherwise, another standard surgical excision is typically performed.

If cancer still remains and more surgery is not possible, a discussion between different cancer doctors to consider next steps is recommended. Treatment may include radiation therapy with or without systemic therapy. If systemic therapy is planned, platinum-based chemotherapy is a recommended option for use with radiation. As with other treatments, enrolling in a clinical trial for systemic therapy is also an option. A clinical trial could also involve treatment with chemotherapy, targeted therapy, or immunotherapy.

If radiation therapy is not expected to kill the cancer completely or may damage critical healthy organs, systemic therapy alone is recommended. Immunotherapy with an immune checkpoint inhibitor is a recommended treatment option if you are eligible. Enrolling in a clinical trial for systemic therapy is also an option.

### If surgery is not an option

If you are not a candidate for surgery, radiation therapy is typically used instead. Systemic therapy may be given in addition to radiation. If systemic therapy is planned, platinum-based chemotherapy is a recommended option for use with radiation.

If radiation therapy is not expected to kill the cancer completely or may damage critical healthy organs, systemic therapy alone is recommended. If you are eligible, immunotherapy with an immune checkpoint inhibitor is a recommended treatment option. Enrolling in a clinical trial for systemic therapy is also an option.

➲ *See Part 5: When treatment is over for information on monitoring and follow-up care.*

## Key points

- Squamous cell skin cancer that has not spread to nearby lymph nodes is known as “local”.
- Local CSCC is most often treated with surgery.
- Key features of the cancer will be considered to determine if it is a low-, high- or very high-risk CSCC. This is called a risk assessment.
- The risk level or category for skin cancer is usually based on the highest risk factor found.
- If the tumor has grown into a nerve or group of nerves, usually seen under the microscope, it is a high-risk or very high-risk cancer.
- The tumor grade is a rating of how fast your doctors expect the cancer to grow and spread.
- The deeper the tumor has invaded into the skin, the higher the risk of the cancer returning after treatment.
- Recommended types of surgery for local, low-risk CSCC include curettage and electrodesiccation (C&E), standard surgical excision, or Mohs surgery or another form of PDEMA.
- For low-risk CSCC in non-surgical candidates, treatment with radiation therapy is an option.
- Recommended types of surgery for local, high-risk or very high-risk CSCC include Mohs surgery/PDEMA and standard surgical excision.
- For high-risk or very high-risk CSCC in non-surgical candidates, treatment with radiation therapy and/or systemic therapy is an option.

# 4

# Regional CSCC (in lymph nodes)


31 Testing

32 Treatment

33 Metastatic squamous cell skin cancer

33 Key points

**Squamous cell carcinoma that has spread to nearby lymph nodes is known as “regional”. The goal of testing for regional cancer will be to see how and where the cancer has spread, so your care team can determine the best treatment plan.**

# Testing

## Biopsy

If lymph nodes near the CSCC feel swollen or look abnormal on initial imaging tests, the next step is a biopsy. The types of biopsies used for squamous cell skin cancer are fine-needle aspiration (FNA) and core needle biopsy. FNA is also known simply as needle biopsy.

## Imaging

If biopsy results confirm that the cancer has spread to nearby lymph nodes, a computed tomography (CT) scan of lymph nodes near the CSCC is recommended. The goal is to learn about the number, location, and size of the lymph nodes with cancer.

More advanced imaging tests like a PET/CT, that uses special injectable agents to detect cancer, may be needed to see if cancer has spread farther than the lymph nodes, or to help plan treatment.

## Surgical evaluation

The results of testing will be considered in order to determine if you are a candidate for surgery to remove the cancerous lesion and nearby lymph nodes.

### Know your options

**It is always important to discuss with your doctor and care team about what your treatment options are, and any preferences or concerns you might have.**



# Treatment

Surgery is recommended to treat squamous cell skin cancer that has spread to nearby lymph nodes. Surgery for regional CSCC involves excision (removal) of the cancerous lesion and nearby lymph nodes. Although surgery is preferred, it may not be an option for one or more reasons. In this case, see **If surgery is not an option** below for information.

If surgery is very risky or might not completely remove your cancer, your doctor may suggest immunotherapy with cemiplimab-rwlc (Libtayo) first. It may shrink the tumor and make surgery less risky.

## Head and neck tumors

Lymph nodes may be removed from one or both sides of the neck during surgery for head and neck tumors. The extent of surgery depends on the number, location, and size of the lymph nodes with cancer. After surgery, radiation therapy is often given to decrease the chance of the tumor returning.

Systemic therapy is sometimes used in addition to radiation therapy after surgery. This may be the case if:

- Lymph nodes with cancer were not removed during surgery, or
- Cancer was found to have grown through the protective outer layer of any lymph nodes removed during surgery (called extracapsular or extranodal extension)

In either of these situations, a discussion between different cancer doctors is recommended. If systemic therapy is planned, platinum-based chemotherapy is preferred for use with radiation if you can have it.

## Tumors on other areas of the body

Surgery is the best way to treat tumors that have spread to other areas of the body if possible. Surgery removes the tumor and nearby lymph nodes. Radiation therapy may be given after surgery to kill leftover cancer cells. This is important if there was more than one lymph node with cancer, or if cancer was found to have grown through the protective outer layer of any lymph nodes removed during surgery.

## If surgery is not an option

If you cannot have surgery, a discussion between different cancer doctors to consider your treatment options is recommended. If you can have it, radiation therapy with or without systemic therapy is recommended. Platinum-based chemotherapy is a recommended option for use with radiation.

If radiation therapy is not expected to kill the cancer completely or may damage healthy organs, systemic therapy alone is recommended. If you are eligible, immunotherapy with an immune checkpoint inhibitor is preferred. Enrolling in a clinical trial may also be an option. A clinical trial could involve treatment with chemotherapy, targeted therapy, or immunotherapy.

If you are not eligible for an immune checkpoint inhibitor or a clinical trial, options for systemic therapy include platinum-based chemotherapy and targeted therapy.

➲ *See Part 6: When treatment is over for information on monitoring and follow-up care.*

# Metastatic squamous cell skin cancer

Cancer cells can spread through blood and lymph to form tumors in other areas of the body. This is called metastasis. Squamous cell skin cancer does not metastasize often. For this reason, there is not much research on the best way to treat metastatic squamous cell skin cancer. A discussion between different cancer doctors is recommended to consider your treatment options.

If surgery and/or radiation therapy cannot remove metastatic CSCC, systemic therapy is recommended. If you are eligible, immunotherapy with an immune checkpoint inhibitor is preferred. Enrolling in a clinical trial for systemic therapy is another option. A clinical trial could involve treatment with chemotherapy, targeted therapy, or immunotherapy.

If you are not eligible for an immune checkpoint inhibitor or a clinical trial, options for systemic therapy include platinum-based chemotherapy and targeted therapy.

## Help for symptoms

Radiation therapy and/or surgery may be used to treat distant tumors that are causing pain or other bothersome side effects. Stereotactic body radiotherapy (SBRT) is a special radiation technique that may be used in some cases. It sends high doses of radiation to small areas to kill cancer cells and is typically given over 3 to 5 treatments.

# Key points

- Squamous cell skin cancer that has spread to nearby lymph nodes is called “regional”.
- Your care team will test suspicious lymph nodes to determine how far the disease has spread.
- Testing could also include scans of your upper body, stomach, and pelvis to check for any metastatic disease (spread) to those areas.
- The best way to treat regional CSCC is with surgery to remove the tumor and nearby lymph nodes.
- Radiation therapy with or without systemic therapy is often given after surgery to kill leftover cancer cells.
- If surgery is not possible or not recommended, radiation therapy, systemic therapy, or a combination of both may be options.
- If radiation therapy is not expected to kill the cancer completely or may harm critical healthy organs, systemic therapy alone is recommended.
- Although it is uncommon, squamous cell skin cancer can metastasize. Metastatic CSCC that cannot be removed with surgery and/or radiation is treated with systemic therapy.
- Systemic therapy options for metastatic CSCC include immunotherapy or a systemic therapy given in a clinical trial. If you are not a candidate for either of these, your doctor may recommend platinum-based chemotherapy or targeted therapy.

# 5
# When treatment is over


35 Skin exams by your doctor

37 Prevention for patients at high-risk

38 Steps you can take

39 Key points

**You've finished treatment. Now you may be wondering if—or when—cancer might return. Because you've already had squamous cell skin cancer, you are at higher risk of getting it again. You're also at higher risk of getting other types of skin cancer. This chapter explains how you can help prevent and detect future skin cancers.**

## Skin exams by your doctor

After finishing treatment, getting regular skin exams to monitor for the return of squamous cell skin cancer is very important. These follow-up exams should include a complete check of the skin on your entire body, as well as the lymph nodes closest to the cancer site. You will be asked to undress and put on a paper gown or drape. Undergarments can be worn during the exam. The gown will be adjusted to allow your doctor to see different areas.

How often you should be checked depends on whether the cancer was local (not in nearby lymph nodes) or regional (in nearby lymph nodes).

For local CSCC, monitoring during the first 2 years after treatment is the most important. Exams should occur at least every 3 to 12 months (for patients who are low risk) or every 3 to 6 months (for patients who are high risk) during this time. If no further skin cancer develops in the first 2 years, then exams are spaced out to every 6 to 12 months (once or twice a year) for another 3 years. After that, having an exam once a year for the rest of your life is recommended by NCCN experts.

For very high-risk local CSCC, exams should occur every 3 to 6 months during the first 2 years, then every 6 months for the next 3

### Skin exams by your doctor

**After finishing treatment, you should have your skin examined by a doctor on a regular basis. How often you should have skin exams depends on whether cancer has spread to nearby lymph nodes.**



years. After that, exams can be spaced out to every 6 to 12 months (once or twice a year) for the rest of your life, as recommended by NCCN experts.

In addition, imaging tests may be used to monitor some people who have local CSCC.

For regional CSCC, physical exams with skin checks should be performed every 2 to 3 months for 1 year, every 2 to 4 months for the second year, every 4 to 6 months for another 3 years, and then every 6 to 12 months for the rest of your life. For patients with regional CSCC, your doctor may want you to have CT scans on a regular basis to look for signs of cancer in nearby lymph nodes or in other parts of your body.

The follow-up exam schedules for both local and regional squamous cell skin cancer are shown in **Guide 1**.

**Guide 1**
**Follow-up exam schedule**

| | |
|---|---|
| **Low-risk local CSCC (no spread to lymph nodes)** | • First 2 years after treatment: Exam every 3 to 12 months<br>• Next 3 years after treatment: Exam every 6 to 12 months<br>• After that: Exam once a year (every 12 months) for life |
| **High-risk local CSCC (no spread to lymph nodes)** | • First 2 years after treatment: Exam every 3 to 6 months<br>• Next 3 years after treatment: Exam every 6 to 12 months<br>• After that: Exam once a year (every 12 months) for life |
| **Very high-risk local CSCC (no spread to lymph nodes)** | • First 2 years after treatment: Exam every 3 to 6 months<br>• Next 3 years after treatment: Exam every 6 months<br>• After that: Exam every 6 to 12 months (once or twice a year) for life |
| **Regional CSCC (spread to lymph nodes)** | • First year after treatment: Exam every 2 to 3 months<br>• Second year after treatment: Exam every 2 to 4 months<br>• Next 3 years after treatment: Exam every 4 to 6 months<br>• After that: Exam every 6 to 12 months (once or twice a year) for life |

# Prevention for patients at high-risk

Treating squamous cell skin cancer when it first appears can help prevent the cancer from growing into deeper layers of the skin. In people who form CSCCs very easily, however, treatment alone may not be the best strategy. Rather than wait for the cancer to form, there are ways to help prevent squamous cell skin cancer if you are considered at high risk.

## Dermatology checks

Following up with a dermatologist for checkups is strongly recommended if you have any of the following conditions:

- Past or current solid organ, marrow, or stem cell transplant
- One or more cutaneous melanomas within the past 5 years
- Four or more nonmelanoma skin cancers in the past 5 years

## Medication

Studies where medications were given to help prevent squamous cell skin cancer from forming have been shown to help:

- People who had an organ transplant
- People who have genetic syndromes that make them more likely to develop CSCCs
- People who have psoriasis who have had psoralen and ultraviolet A (PUVA) therapy
- People who have had squamous cell skin cancer more than once
- People who have large areas of actinic keratosis

Some medicines used to help stop squamous cell skin cancer from forming are described next.

### Oral retinoids

When taken by mouth (orally), drugs called retinoids can help prevent squamous cell carcinoma from forming in people who form actinic keratoses easily. Acitretin (Soriatane) and isotretinoin are two retinoids used for this purpose.

Oral retinoids can cause drying or chapping of the lips, peeling of the skin, hair disorders, and more extreme side effects. They can also cause birth defects, and should therefore be used with extreme caution in people who could become pregnant. People taking these drugs need to have their blood tested on a regular basis.

### Oral nicotinamide

Nicotinamide is a form of niacin (vitamin B3). Nicotinamide supplements are used to treat skin conditions and niacin deficiencies. Nicotinamide may help prevent squamous cell carcinoma from returning after treatment and from spreading to distant sites in people at high risk.

To prevent squamous cell skin cancer, nicotinamide is taken orally (by mouth) twice a day. No prescription is needed for nicotinamide and it is considered safe.

Nicotinamide can also be made in the body by eating niacin-rich foods such as fish, chicken or other poultry, nuts, legumes (beans), eggs, and cereal grains.

# Steps you can take

Your care team should provide you with information about how you can play a role in preventing new skin cancers from forming. The information should cover two important topics—sun protection and skin self-exams.

## Sun protection

Protecting your skin from the sun is an important part of preventing future squamous cell carcinomas. One of the best ways to do this is to use a broad-spectrum sunscreen with a sun protection factor (SPF) of 30 or higher.

When spending time outside, sunscreen should be reapplied to all exposed areas every 2 hours, or after swimming or sweating. Consider also using a face moisturizer with a SPF of 30 or higher on a daily basis.

Physically shielding your skin from the sun with hats and clothing can help protect it. Similar to SPF ratings for sunscreen, clothing with an ultraviolet protection factor (UPF) rating is available. The higher the UPF rating, the better the sun protection.

Staying inside or in the shade during peak daylight hours is another way to protect your skin. You should never use tanning booths or beds. Your goal is to never get another sunburn or suntan.

## Skin self-exams

Your doctor should also teach you how to examine your skin yourself for signs of cancer. Following the same process each time can make it easier to notice any changes from the last time you checked. A handheld mirror is helpful for seeing hard-to-reach areas. You may also ask a spouse or friend to help you do the exam.

Ideally, you should do a self-exam once a month. If you had regional CSCC, meaning that the cancer spread to nearby lymph nodes, your doctor should also teach you how to inspect your lymph nodes for signs of cancer.

### Sun protection

**When spending time outside, apply a sunscreen with SPF 30 or higher. Sunscreen should be reapplied to all exposed areas every 2 hours, or after swimming or sweating. Consider using a face moisturizer with SPF 30 or higher on a daily basis.**



# Key points

- After treatment for CSCC, it's important to have your skin examined by your doctor on a regular basis. How often exams are needed depends on whether cancer has spread to nearby lymph nodes.
- People at high risk of getting squamous cell skin cancer may benefit from medicines or topical treatments that can help prevent skin cancers from forming.
- Using broad-spectrum sunscreen daily, wearing protective clothing, and staying out of the sun are steps you can take to help prevent new skin cancers from forming.
- In addition to skin checks by your doctor, patients should examine their skin themselves for signs of skin cancer on a regular basis. Patients with regional CSCC should also examine their lymph nodes.

## Should I be concerned about getting more CSCCs?

Out of 100 people who have had squamous cell skin cancer, about 40 (40%) will get a new CSCC within 5 years--and most will get one within 2 years. For this reason, monitoring during the first 2 years after treatment is very important.

NCCN experts recommend having regular skin exams by your doctor, doing your own skin self-exams, and protecting your skin from the sun and UV rays.

### Skin self-exams

**In addition to getting full skin exams by your doctor, examining your skin yourself on a regular basis can help spot the return of cancer and help find new cancers early.**



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# Making treatment decisions

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**It is important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.**

# It's your choice

In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your team.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your team, it will help you feel supported when considering options and making treatment decisions.

## Second opinions

It is normal to want to start treatment as soon as possible. While cancer should not be ignored, there is time to have another cancer care provider review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

## Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

# Questions to ask

Possible questions to ask your cancer care team are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

# Questions about cancer testing

1. What tests will I have?
2. Do the tests have any risks?
3. Will my insurance pay for all of the tests you are recommending?
4. Do I need to do anything to prepare for testing?
5. Should I bring someone with me to the appointments?
6. Where do I go for testing, and how long will it take?
7. If any of the tests will hurt, what will you do to make me comfortable?
8. How soon will I know the results and who will explain them to me?
9. How can I get a copy of the pathology report and other test results?
10. Is there an online portal with my test results?

# Questions about treatment options

1. What are my treatment options?
2. Is a clinical trial an option for me?
3. What will happen if I do nothing?
4. Are you suggesting options other than what NCCN recommends? If yes, why?
5. How do my age, sex, overall health, and other factors affect my options?
6. What if I am pregnant, or planning to become pregnant?
7. Does any option offer a cure or long-term cancer control?
8. What are the side effects of the treatments?
9. How do I get a second opinion?
10. How long do I have to decide about treatment, and is there a social worker or someone who can help me decide?

# Questions about what to expect

1. Does this hospital or cancer center offer the best treatment for me?
2. Do I have a choice of when to begin treatment?
3. How long will treatment last?
4. Will my insurance cover the treatment you're recommending?
5. Are there any programs to help pay for treatment?
6. What supportive care and services are available to me and my caregivers?
7. Who should I contact with questions or concerns if the office is closed?
8. How will you know if the treatment is working?
9. What are the chances of the cancer worsening or returning?
10. What follow-up care is needed after treatment?

# Questions about side effects

1. What are the possible complications and side effects of treatment?
2. Does the cancer itself cause any side effects?
3. Which side effects are most common and how long do they usually last?
4. Which side effects are serious or life-threatening?
5. Are there any long-term or permanent side effects?
6. What symptoms should I report right away, and who do I contact?
7. What can I do to prevent or relieve the side effects of treatment?
8. Do any medications worsen side effects?
9. Do any side effects lessen or worsen in severity over time?
10. Will you stop or change treatment if there are serious side effects?

# Questions about clinical trials

1. Do you recommend that I consider a clinical trial for treatment?
2. How do I find clinical trials that I can participate in?
3. What are the treatments used in the clinical trial?
4. Has the treatment been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect and how will they be managed?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this doesn't work?
9. How will you know if the treatment is working?
10. Will the clinical trial cost me anything?

# Questions about your care team’s experience

1. Are you board certified? If yes, in what area?
2. What is your experience as well as your team's experience with treating the type of cancer I have?
3. How many patients like me (of the same age, gender, race) have you treated?
4. Will you be consulting with experts to discuss my care? Whom will you consult?
5. Is this treatment (or procedure) a major part of your practice? How often have you done this treatment (or procedure) in the last year?
6. How many of your patients have had complications? What were the complications?

# Resources

**NCCN Patient and Caregiver Resources**
NCCN.org/patientresources

**Save Your Skin Foundation**
saveyourskin.ca/

**Skin Cancer Education & Research Foundation**
skincancerinfo.org/

**The Skin Cancer Foundation**
skincancer.org

**Triage Cancer**
triagecancer.org

**U.S. National Library of Medicine Clinical Trials Database**
clinicaltrials.gov



**Let us know what you think!**

**Please take a moment to complete an online survey about the NCCN Guidelines for Patients.**

**NCCN.org/patients/response**



# Words to know

**actinic keratosis**
An area of scaly skin that may become squamous cell skin cancer, but this change is uncommon. Also called solar keratosis.

**albinism**
Lack of color in the hair, skin, and eyes.

**basal cell carcinoma**
The most common type of skin cancer. Also called basal cell skin cancer.

**biopsy**
A procedure that removes fluid or tissue samples to be tested for a disease.

**brachytherapy**
A type of radiation therapy used to treat superficial skin cancers that places the radioactive source in close proximity to the tumor.

**clinical trial**
A type of research that assesses how well health tests or treatments work in people.

**computed tomography (CT)**
A test that uses x-rays from many angles to make a picture of the insides of the body.

**cryotherapy**
A procedure that freezes and destroys precancerous and cancerous cells using a very cold liquid or tool. Also called cryosurgery.

**curettage and electrodesiccation (C&E)**
A procedure used to treat skin cancer by scraping away cancerous tissue and destroying remaining cancer cells with an electric needle.

**dermis**
The second layer of skin that is beneath the outer layer. Contains hair follicles, nerves, sweat glands, oil glands, and blood vessels.

**epidermis**
The top layer of skin, where squamous cells and basal cells are found.

**external beam radiation therapy (EBRT)**
A cancer treatment with radiation delivered from a machine outside the body.

**hyperkeratosis**
Thickening of the outer layer of skin.

**hypodermis (subcutis)**
The deepest layer of skin, made up of fat and connective tissue.

**immunotherapy**
A cancer treatment that stimulates the activity of your body's immune system. By doing so, it improves your body's ability to find and destroy cancer cells.

**local therapy**
A treatment that is given to a confined area.

**Marjolin's ulcer**
Squamous cell skin cancer that forms in an area of wounded, inflamed, or scarred skin.

**metastasis**
When cancer cells spread through blood and lymph to form tumors in other areas of the body.

**Mohs surgery**
The most common form of peripheral and deep en face margin assessment (PDEMA), a procedure that is used to treat skin cancer.

**peripheral and deep en face margin assessment (PDEMA)**
Layers of cancer-containing tissue are removed and examined under a microscope until all cancer tissue has been removed. Also called Mohs micrographic surgery.

**photodynamic therapy (PDT)**
Treatment with drugs that may kill cancer cells when exposed to light.

**primary treatment**
The main treatment used to rid the body of cancer.

**radiation therapy**
A treatment that uses intense energy to kill cancer cells. Also called radiotherapy.

**SCC in situ**
A very early form of squamous cell skin cancer marked by scaly or thickened patches on the skin. Also called Bowen's disease.

**squamous cell skin cancer**
The second most common type of skin cancer, most often caused by many years of sun exposure or multiple sunburns. Also called cutaneous squamous cell carcinoma (cSCC).

**stereotactic body radiotherapy (SBRT)**
A radiation technique that uses high doses of radiation to small areas to kill cancer cells.

**subcutaneous tissue**
The layer of skin below the dermis that is known for its many fat cells. Also called hypodermis.

**sun protection factor (SPF)**
A rating of protection against ultraviolet rays.

**surgical margin**
The normal-looking ring of tissue around a tumor that is removed during surgery.

**systemic therapy**
A type of treatment that works throughout the body.

**targeted therapy**
A cancer treatment that may target and attack specific types of cancer cells.



## We want your feedback!

**Our goal is to provide helpful and easy-to-understand information on cancer.**

**Take our survey to let us know what we got right and what we could do better.**

**NCCN.org/patients/feedback**

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Squamous Cell Skin Cancer, Version 1.2023 – March 10, 2023. It was adapted, reviewed, and published with help from the following people:

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# NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
*Philadelphia, Pennsylvania*
*800.789.7366 • pennmedicine.org/cancer*

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
*Cleveland, Ohio*
*UH Seidman Cancer Center*
*800.641.2422 • uhhospitals.org/services/cancer-services*
*CC Taussig Cancer Institute*
*866.223.8100 • my.clevelandclinic.org/departments/cancer*
*Case CCC*
*216.844.8797 • case.edu/cancer*

City of Hope National Medical Center
*Duarte, California*
*800.826.4673 • cityofhope.org*

Dana-Farber/Brigham and Women's Cancer Center |
Massachusetts General Hospital Cancer Center
*Boston, Massachusetts*
*617.732.5500 • youhaveus.org*
*617.726.5130 • massgeneral.org/cancer-center*

Duke Cancer Institute
*Durham, North Carolina*
*888.275.3853 • dukecancerinstitute.org*

Fox Chase Cancer Center
*Philadelphia, Pennsylvania*
*888.369.2427 • foxchase.org*

Fred & Pamela Buffett Cancer Center
*Omaha, Nebraska*
*402.559.5600 • unmc.edu/cancercenter*

Fred Hutchinson Cancer Center
*Seattle, Washington*
*206.667.5000 • fredhutch.org*

Huntsman Cancer Institute at the University of Utah
*Salt Lake City, Utah*
*800.824.2073 • huntsmancancer.org*

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
*Indianapolis, Indiana*
*888.600.4822 • www.cancer.iu.edu*

Mayo Clinic Comprehensive Cancer Center
*Phoenix/Scottsdale, Arizona*
*Jacksonville, Florida*
*Rochester, Minnesota*
*480.301.8000 • Arizona*
*904.953.0853 • Florida*
*507.538.3270 • Minnesota*
*mayoclinic.org/cancercenter*

Memorial Sloan Kettering Cancer Center
*New York, New York*
*800.525.2225 • mskcc.org*

Moffitt Cancer Center
*Tampa, Florida*
*888.663.3488 • moffitt.org*

O'Neal Comprehensive Cancer Center at UAB
*Birmingham, Alabama*
*800.822.0933 • uab.edu/onealcancercenter*

Robert H. Lurie Comprehensive Cancer
Center of Northwestern University
*Chicago, Illinois*
*866.587.4322 • cancer.northwestern.edu*

Roswell Park Comprehensive Cancer Center
*Buffalo, New York*
*877.275.7724 • roswellpark.org*

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
*St. Louis, Missouri*
*800.600.3606 • siteman.wustl.edu*

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
*Memphis, Tennessee*
*866.278.5833 • stjude.org*
*901.448.5500 • uthsc.edu*

Stanford Cancer Institute
*Stanford, California*
*877.668.7535 • cancer.stanford.edu*

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
*Columbus, Ohio*
*800.293.5066 • cancer.osu.edu*

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
*Baltimore, Maryland*
*410.955.8964*
*www.hopkinskimmelcancercenter.org*

The UChicago Medicine Comprehensive Cancer Center
*Chicago, Illinois*
*773.702.1000 • uchicagomedicine.org/cancer*

The University of Texas MD Anderson Cancer Center
*Houston, Texas*
*844.269.5922 • mdanderson.org*

UC Davis Comprehensive Cancer Center
*Sacramento, California*
*916.734.5959 • 800.770.9261*
*health.ucdavis.edu/cancer*

UC San Diego Moores Cancer Center
*La Jolla, California*
*858.822.6100 • cancer.ucsd.edu*

UCLA Jonsson Comprehensive Cancer Center
*Los Angeles, California*
*310.825.5268 • cancer.ucla.edu*

UCSF Helen Diller Family Comprehensive Cancer Center
*San Francisco, California*
*800.689.8273 • cancer.ucsf.edu*

University of Colorado Cancer Center
*Aurora, Colorado*
*720.848.0300 • coloradocancercenter.org*

University of Michigan Rogel Cancer Center
*Ann Arbor, Michigan*
*800.865.1125 • rogelcancercenter.org*

University of Wisconsin Carbone Cancer Center
*Madison, Wisconsin*
*608.265.1700 • uwhealth.org/cancer*

UT Southwestern Simmons Comprehensive Cancer Center
*Dallas, Texas*
*214.648.3111 • utsouthwestern.edu/simmons*

Vanderbilt-Ingram Cancer Center
*Nashville, Tennessee*
*877.936.8422 • vicc.org*

Yale Cancer Center/Smilow Cancer Hospital
*New Haven, Connecticut*
*855.4.SMILOW • yalecancercenter.org*




**Take our survey, and help make the NCCN Guidelines for Patients better for everyone!**

**NCCN.org/patients/comments**

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# Squamous Cell Skin Cancer

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