Cervical Cancer
It's easy to get lost in the cancer world

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- Step-by-step guides to the cancer care options likely to have the best results
- Based on treatment guidelines used by health care providers worldwide
- Designed to help you discuss cancer treatment with your doctors
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# Cervical cancer basics

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Cervical cancer basics

Cervical cancer is a common cancer of the female reproductive system. Most cervical cancers are caused by long-term infection with human papillomavirus (HPV). HPV is the most common sexually transmitted infection (STI). The use of Pap smears has resulted in much lower rates of cervical cancer in the United States.

The cervix

The cervix (also called the uterine cervix) is the narrow, lower end of the uterus. The uterus is where a baby grows and develops before being born. During birth, the cervix opens (dilates) and thins (effaces) to allow the baby to move into the vagina. The vagina, or birth canal, is the muscular passage through which babies are born.

An ovary and a fallopian tube are on each side of the upper uterus. The fallopian tubes connect to the top part of the uterus. The ovaries make eggs for sexual reproduction. They also make hormones that affect breast growth, body shape, and the menstrual cycle. Eggs pass out of the ovary and travel through the attached fallopian tube into the uterus. The cervix, uterus, vagina, ovaries, and fallopian tubes are part of the female reproductive system.

To understand cervical cancer, it helps to understand the structure of the cervix. The ectocervix and endocervix are the thin layer of tissue that lines the outer part and inner

The reproductive system

The reproductive system is a group of organs that work together for the purpose of sexual reproduction. In addition to the uterus (and cervix), this system includes the ovaries, fallopian tubes, and vagina.
parts of the cervix. The cervical stroma is the thick layer of muscular tissue beneath the cervical lining. The parametrium is the fat and connective tissue that surrounds the uterus (and cervix) and connects it to the pelvis.

Most cervical cancers start in the lining of the cervix. The ectocervix is the outer part of the cervix. It appears rounded and extends into the vagina. The ectocervix can be seen during an examination of the vagina and cervix using a tool called a speculum. It is lined with cells called squamous cells. In the center of the ectocervix is a narrow opening called the external os. During menstruation, the external os opens slightly to allow blood to pass into the vagina.

The endocervix (endocervical canal) is the inner part of the cervix that forms a canal between the vagina and the body of the uterus. The endocervix is lined with columnar (glandular) cells that make mucus. The inner os is the upper part of the endocervix that serves as an opening between the uterus and the cervix.

The area where the endocervix and ectocervix meet is called the squamo-columnar junction or the transformation zone. Most cervical cancers and pre-cancers start in the ectocervix portion of the transformation zone.

Although the cervix is part of the uterus, uterine cancer is diagnosed and treated differently than cervical cancer. This patient guide does not discuss treatment of uterine cancers, such as endometrial cancer and uterine sarcomas.

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The ectocervix

This rounded, outer part of the cervix can be seen during a gynecologic exam. The small opening in the ectocervix is called the external os. Sperm enter the uterus through the external os.
The start of cervical cancer

Cervical cancer starts as areas of abnormal, microscopic cells on the surface of the cervix. These changes are known as cervical dysplasia or cervical intraepithelial neoplasia (CIN). Mutations (changes) in the DNA of these cells cause them to become abnormal and potentially cancerous. If left untreated, cervical dysplasia may become cervical cancer.

CIN is graded based on how abnormal the cells look when viewed under a microscope. The possible grades are 1, 2, or 3. The lower the grade, the less abnormal the cells. Cervical dysplasia becomes cancer when the abnormal cells invade the muscular tissue beneath the cervical lining (the cervical stroma).

An area of dysplasia or cancer is also referred to as a lesion. Low-grade squamous intraepithelial lesion (LSIL) refers to mild dysplasia (CIN 1). High-grade squamous intraepithelial lesion (HSIL) refers to moderate or severe dysplasia (CIN 2 and 3). HSIL is considered a pre-cancer.

Cervical changes

Cervical dysplasia refers to areas of abnormal cells on the lining of the cervix. Low-grade squamous intraepithelial lesion (LSIL) refers to mild dysplasia (CIN 1). High-grade squamous intraepithelial lesion (HSIL) refers to moderate or severe dysplasia (CIN 2 and 3). HSIL is considered a pre-cancer.
Risk factors

A risk factor is something that increases the risk of developing a disease. Some people with no known risk factors may develop cervical cancer, while others with risk factors may not.

HPV infection

Almost all cervical cancers are caused by long-term infection with HPV. HPV is an extremely common sexually transmitted infection (STI). Most sexually active people have or had HPV at one point. Most are unaware that they are or were infected.

In most people, the immune system gets rid of (“clears”) HPV from the body. In other people, the virus causes long-term cell changes that develop into cancer. The progression to cancer often occurs decades after the initial infection. Doctors are still learning why one person gets cervical cancer and another does not. Other types of cancer caused by HPV include anal, head and neck, penile, vaginal, and vulvar cancers.

There are more than 100 types (strains) of HPV. Infection with some strains is more likely to lead to cancer. High-risk forms of HPV include HPV-16 and HPV-18. Other HPV types can cause abnormal skin growths, called warts, to form on the anus, genitals, or other areas of the body.

A vaccine that protects against 9 different strains of HPV, including the highest-risk strains, is available in the United States. While previously only recommended for routine use in adolescents and young adults, vaccination is now an option for adults aged 45 and under.

There are two other HPV vaccines available in other parts of the world. One protects against HPV-16 and HPV-18 only. The other targets these highest-risk strains as well as two additional types.

The vaccine is most effective in younger people (ideally under age 13) because they are less likely to have been exposed to HPV. Also, while the vaccine can prevent new HPV infections, it does not treat existing HPV infections or HPV-related cancer.

Other risk factors

Other risk factors for cervical cancer are listed below. Some of these lead to a higher risk because they either increase the risk of being exposed to HPV or they weaken the immune system, which can make it harder for the body to clear HPV infection.

- A history of smoking
- Having given birth more than once (called “high parity” or multiparity)
- Oral contraceptive (birth control) use
- Being sexually active at an early age
- A high number of sexual partners
- A history of sexually transmitted infection
- Certain autoimmune diseases
- A weakened immune system due to human immunodeficiency virus (HIV) or AIDS, for example
Types of cervical cancer

Most cervical cancers start in the ectocervix. The ectocervix is lined with squamous cells. Cancer that forms in squamous cells is called a squamous cell carcinoma.

About 2 out of 10 cervical cancers form in the endocervical canal. The endocervix is lined with cells that make mucus. These cells are referred to as glandular, gland-like, secretory, or columnar cells. Cancers that form in glandular cells are called adenocarcinomas.

Less commonly, the cancer may contain both squamous and adenocarcinoma cells. These cancers are referred to as adenosquamous carcinomas. They are sometimes called “mixed” tumors.

Treatment for squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma is the focus of Part 4.

The rarest and most aggressive type of cervical cancer is neuroendocrine carcinoma of the cervix (NECC). Treatment for small cell NECC is the focus of Part 5.

This patient guide does not discuss other types of cervical cancer such as glassy-cell carcinomas, sarcomas, or other tumor (histologic) types.
Key points

- The cervix is the lower, narrow part of the uterus that connects the uterus to the vagina.

- The rounded, outer part of the cervix that extends into the vagina is called the ectocervix.

- The narrow opening in the center of the ectocervix is the external os. It allows fluids to pass between the vagina and uterus.

- The endocervix is the canal between the vagina and the body of the uterus.

- The area where the endocervix and ectocervix meet is called the squamo-columnar junction or the transformation zone.

- Most cervical cancers and pre-cancers start in the ectocervix portion of the transformation zone.

- Squamous cell carcinoma is the most common type of cervical cancer, followed by adenocarcinoma. Adenosquamous carcinomas are less common.

- Neuroendocrine carcinoma of the cervix (NECC) is a rare and aggressive type of cervical cancer.

- The risk factor most strongly linked with cervical cancer is long-term infection with HPV. HPV is a very common sexually transmitted infection.
2 Testing and staging

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Your doctors will make a treatment plan just for you. First, they will need to gather information about the cancer and your general health. This chapter describes testing you may have and other steps needed to create your treatment plan.

Biopsy

**Cervical biopsy and pathologic review**
A cervical biopsy involves removing small samples of tissue from the cervix. It is the most commonly used procedure to diagnose cervical cancer. Samples may be taken from the rounded, bottom part of the cervix (ectocervix) and/or from the endocervical canal.

The removed tissue is examined by a specialized doctor called a pathologist. The pathologist looks for abnormal areas, including areas of cancer or pre-cancer. The pathologist also determines the type of cervical cancer, when possible.

**Cervical biopsy**

A cervical biopsy is the most commonly used procedure to diagnose cervical cancer. A small sample of tissue is removed from the ectocervix (shown here on left) and/or the endocervix (shown here on right).
Cone biopsy can be both a test and a treatment. It may be used to gather more information about the extent of the cancer after a cervical biopsy. It is also a recommended treatment option for some early cervical cancers.

Also known as cervical conization, cone biopsy involves removing a cone-shaped portion of the cervix. The cone-shaped sample includes tissue from both the ectocervix and the endocervical canal. All of the transformation zone—where the ectocervix and endocervix meet—is removed. Most cervical cancers start in this area.

Most commonly, a technique called cold knife conization (CKC) is used. In this method a surgical scalpel is used to remove the tissue. In some cases loop electrosurgical excision procedure (LEEP) may be performed instead. In LEEP, a thin loop of electrified (heated) wire is used instead of a scalpel to cut out the cervical tissue.

After removing the cone-shaped sample of tissue, your doctor may use a spoon-shaped tool called a curette to scrape a sample of tissue from the cervical canal. This is called endocervical curettage.

The tissue removed during a cone biopsy is examined under a microscope by a pathologist. A pathologist is a doctor who specializes in evaluating cells and tissues to diagnose disease.

Cone biopsy

A cone biopsy removes a cone-shaped section of the cervix that includes the transformation zone. Cone biopsy may be the only treatment needed for some early-stage cervical cancers.
Health history and physical exam

To help plan treatment, expect your doctor to ask about your past and current health, including:

- Illnesses, diseases, and surgeries
- Medicines that you take (prescription or over-the-counter)
- Your lifestyle (your diet, how much exercise you get, whether you smoke or drink alcohol)
- Symptoms that could be related to cervical cancer, such as watery vaginal discharge

Your doctor will also do a physical exam of your body, which may include:

- Checking your vital signs (blood pressure, heart rate, breathing rate, and body temperature) and assessing your overall appearance
- Feeling and/or listening to the organs in your abdomen, including your liver and stomach
- Performing a pelvic examination to check the size and position of your cervix and uterus

Blood tests

Blood tests provide helpful information about your general health and the health of your liver, kidneys, and other organs before treatment.

A complete blood count (CBC) is a common test that measures the number of red blood cells, white blood cells, and platelets in a sample of blood. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help to control bleeding.

A blood chemistry profile measures the levels of different chemicals in your blood. Chemicals in your blood are affected by your kidneys, bones, and other organs and tissues. Blood chemistry levels that are too high or too low may be a sign that an organ is not working well. Abnormal levels may also be caused by the spread of cancer or by other diseases.

Liver function tests are often done along with a blood chemistry profile. The liver is an organ that does many important jobs, such as remove toxins from the blood. Liver function tests measure enzymes that are made or processed by the liver. Levels that are too high or too low may be a sign of liver damage or cancer spread.

If you have not had a recent human immunodeficiency virus (HIV) test, or have never been tested, your doctor may recommend it. If you have HIV, you are likely to be referred to an HIV specialist. Having HIV should not affect your cancer treatment. The treatment options described in this guide apply to both HIV-positive and HIV-negative patients.
Testing and staging

Imaging

Imaging helps determine the extent of the cancer. The size and spread of the cancer is used to guide treatment.

Computed tomography (CT)
You may have a CT scan of your chest, abdomen, and/or pelvis. A CT scan is a more detailed kind of x-ray. It takes many pictures of an area inside the body from different angles. A computer combines the pictures to make three-dimensional (3-D) images. During the scan, you will lie face up on a table that moves through a large tunnel-like machine. To see everything better, a substance called “contrast” may be injected into your vein and also mixed with a liquid you drink. Contrast makes the CT pictures clearer. The contrast may cause you to feel flushed or get hives. You will be alone during the scan, but a technician will be nearby. You will be able to hear and talk to the technician at all times. You may hear buzzing or clicking during the scan.

PET/CT
A CT scan may be combined with another imaging test called positron emission tomography (PET). PET uses small amounts of radioactive materials called radiotracers. About an hour before the scan, you will be injected with a sugar radiotracer. The radiotracer gives off a small amount of energy that can be seen by the imaging machine. Cancer appears brighter in the pictures because cancer cells use sugar more quickly than normal cells. In some cases, PET may be performed with MRI (described next) instead of CT.
Magnetic resonance imaging (MRI)
MRI uses strong magnetic fields and radio waves to make pictures of areas inside the body. It is especially good at making clear pictures of areas of soft tissue. Unlike a CT scan or x-ray, MRI does not use radiation.

You may have an MRI of your pelvis. An MRI can show the tissues of the uterus, cervix, and vagina closely. An MRI may show whether the cancer has spread to the vagina or other nearby organs.

For those with a rare and aggressive type of cervical cancer called small cell neuroendocrine carcinoma of the cervix (NECC), MRI of the brain is also recommended as part of initial testing.

Getting an MRI scan is similar to getting a CT scan. You will lie face-up on a table that moves through a large tunnel in the scanning machine. The scan may cause your body to feel a bit warm. Like a CT scan, a contrast agent will be used to make the pictures clearer. MRI scans take longer to complete than CT scans. The full exam can take an hour or more. Tell your doctor if you get nervous in tight spaces.

MRI machine
MRI makes pictures of areas inside the body without using radiation. An MRI can show the tissues of the uterus, cervix, and vagina in detail.
Transvaginal ultrasound
If you cannot have MRI of your pelvis, you may have an ultrasound instead. Ultrasound uses sound waves to make pictures of areas inside of the body. It is good at showing the size, shape, and location of the cervix.

In a transvaginal ultrasound, a probe will be inserted into your vagina. This helps your doctor see the cervix and nearby areas more clearly. Ultrasounds are generally painless, but you may feel some discomfort when the probe is inserted.
Other testing and care

Checking the bladder and bowel
Your doctor may want to examine nearby organs, including the bladder and bowel, for signs of cancer. If these tests are needed, expect to receive general anesthesia. This means you will be fully sedated and unaware that the procedure is taking place. These are referred to as examinations under anesthesia (EUAs).

Cystoscopy is a procedure to see inside the bladder and other organs of the urinary tract. It is performed using a hollow tool with a magnifying lens at one end, called a cystoscope. The cystoscope is inserted through the urethra and guided into the bladder.

Proctoscopy is a procedure to see inside the anus and rectum. It is performed with a thin, tube-like instrument with a light and magnifying lens called a proctoscope.

If abnormal or suspicious areas are seen during cystoscopy or proctoscopy, tissue samples will be removed and tested (biopsied).

Discussion of fertility-sparing options
If you want the option of becoming pregnant in the future, you may discuss fertility-sparing treatment options with your doctor. Fertility-sparing treatment involves surgery that spares (does not remove) the uterus. It is typically only an option for smaller cervical cancers. Ask your doctor about your options if you would like to preserve your fertility.

If you become pregnant after fertility-sparing treatment, the decision to have your uterus removed after pregnancy is one that should be made by you and your doctor. If you continue to have abnormal Pap smears or have long-term HPV infection, surgery to remove the uterus is strongly recommended.

A fertility-sparing surgical approach is not appropriate for advanced stages of cervical cancer or for some uncommon types of cervical cancer. If fertility preservation is desired, talk to your doctor about getting the opinion of a reproductive endocrinologist. Reproductive endocrinologists are doctors that specialize in fertility. Although natural pregnancy will not be possible, options to discuss may include ovarian transposition, egg or embryo freezing, and consideration of possible surrogate pregnancy in the future.

Ovarian transposition
Cervical cancer treatment may involve external beam radiation therapy (EBRT). Radiation damages the ovaries and causes them to stop producing hormones needed for natural pregnancy. Ovarian transposition is a surgery that moves one or both ovaries out of the range of the radiation beam. The medical name for this procedure is oophoropexy.

Ovarian transposition before starting EBRT may be an option if you are premenopausal and have the most common type of cervical cancer, squamous cell carcinoma.

Egg freezing
Unfertilized eggs can be removed, frozen, and stored for later use. The medical term for this is oocyte preservation.

Surrogacy
If you have frozen embryos or frozen eggs (oocytes), you may consider using a surrogate. A surrogate volunteers to have the embryos
inserted into her uterus. She carries the pregnancy and gives birth. The surrogate may be a relative or friend.

For more information on fertility preservation, see the NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer at NCCN.org/patientguidelines.

Help to quit smoking
If you are a smoker, now is the time to quit. Quitting can lead to better cancer treatment outcomes. Quitting at any time will greatly benefit your health and can reduce the risk of getting other cancers and serious diseases. Help is available if you are ready to stop smoking. Ask your treatment team about resources and programs that can help you break the habit.

Staging

The results of imaging and other testing described in this chapter are used to determine the stage (extent) of the cancer. Your treatment options will depend on the cancer stage.

The International Federation of Gynecology and Obstetrics (FIGO) system is used to stage cervical cancer. There are four main stages in the FIGO system: I (1), II (2), III (3), and IV (4). The stages are broken down into sub-stages that have letters and may also have a number.

The following information is used to stage the cancer in the FIGO system:

- The size or extent/depth of the tumor
- Whether any lymph nodes have cancer
- Whether the cancer has spread to the liver, lungs, and/or bone (metastasized)

The stages are explained and pictured on the following pages. In general, people with earlier cancer stages have better outcomes, but not always. Some people will do better than expected for their stage, and some will do worse.
Stage IA cervical cancer

The cancer is 5 millimeters (mm) or smaller. 5 mm is about the size of a standard pencil eraser. Cancers 3 mm or smaller are stage IA1. Cancers between 3 and 5 mm are stage IA2.
Stage IB1 cervical cancer

The cancer is larger than 5 mm but smaller than 2 cm.
Stage IB2 and IB3 cervical cancer

The cancer is only in the cervix. In stage IB2, the cancer is between 2 and 4 cm. In stage IB3, the cancer is larger than 4 cm.
Stage II cervical cancer

The cancer has grown beyond the cervix. If the cancer has grown into the upper vagina, the stage is IIA. Stage IIA1 cancers are 4 cm or smaller. Stage IIA2 cancers are larger than 4 cm. Cancer that has grown into the fat and connective tissue that surrounds the cervix and uterus is stage IIB.
Stage IIA cervical cancer

The cancer has grown into the lower third of the vagina.
Stage IIIB cervical cancer

The cancer has grown into the pelvic wall and/or has caused kidney swelling or dysfunction.
Stage IIIC cervical cancer

There is cancer in lymph nodes near the cervix (pelvic lymph nodes) and/or in lymph nodes in the abdomen, called the para-aortic lymph nodes.
Stage IVA cervical cancer

The cancer has spread to nearby organs, such as the bladder or rectum.
Stage IVB cervical cancer

The cancer is metastatic. It has spread to the liver, lungs, abdomen, bone, or other distant sites or lymph nodes.
Cancer care plan

Your treatment team
Treatment for cervical cancer may involve a team of experts, including a gynecologic oncologist, a medical oncologist, and a radiation oncologist.

A gynecologic oncologist is an expert in surgery and chemotherapy for female reproductive cancers. A medical oncologist is an expert in treating cancer with chemotherapy. A radiation oncologist is an expert in the use of radiation therapy to treat cancer.

Your primary care physician (PCP) can also be a part of your team. Your PCP can help you express your feelings about treatments to the team. Treatment of other medical problems may be improved if your PCP is informed of your cancer care. In addition to doctors, you may receive care from nurses, social workers, and other health experts. Ask to have the names and contact information of your health care providers included in the treatment plan.

Cancer treatment
There is no single treatment practice that is best for all patients. There is often more than one treatment option, including clinical trials. Clinical trials study the safety and effectiveness of investigational treatments.

The treatment that you and your doctors agree on should be described in the treatment plan. It is also important to note the goal of treatment and the chance of a good treatment outcome. All known side effects should be listed and the time required to treat them should be noted.

Your treatment team

Treating cervical cancer takes a team of doctors and other experts. Your treatment team may include a:

Gynecologic oncologist: An expert in female reproductive cancers. Many are also medical oncologists.
Pathologist: An expert in evaluating and testing tissue to diagnose and classify disease.
Radiologist: An expert in interpreting imaging tests.
Medical oncologist: An expert in cancer drugs. Many are also experts in gynecologic cancers.
Oncology nurse: A nurse who specializes in treating and caring for people who have cancer.
Oncology pharmacist: A licensed pharmacist with special training in cancer drugs.
Your treatment plan may change because of new information. You may change your mind about treatment. Tests may find new results. How well the treatment is working may change. Any of these changes may require a new treatment plan.

**Stress and symptom control**
Cancer and its treatment can cause bothersome symptoms. The stress of having cancer can also cause symptoms. There are ways to treat many symptoms, so tell your treatment team about any that you have.

Feelings of anxiety and depression are common among people with cancer. At your cancer center, cancer navigators, social workers, and other experts can help. Help can include support groups, talk therapy, or medication. Some people also feel better by exercising, talking with loved ones, or relaxing.

You may be unemployed or miss work during treatment. Or, you may have too little or no health insurance. Talk to your treatment team about work, insurance, or money problems. They will include information in the treatment plan to help you manage your finances and medical costs.

See the *NCCN Guidelines for Patients: Distress During Cancer Care* at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines) for more information.

**Supportive care**
Supportive care is treatment given to relieve the symptoms of cancer or the side effects of cancer treatment. It aims to relieve discomfort and improve quality of life. Supportive care may be given alone or in combination with cancer treatment. It is also referred to as palliative care.

**Advance care planning**
Talking with your doctor about your prognosis can help with treatment planning. If the cancer cannot be controlled or cured, a care plan for the end of life can be made. There are many benefits to advance care planning, including:

- Knowing what to expect
- Making the most of your time
- Lowering the stress of caregivers
- Having your wishes followed
- Having a better quality of life
- Getting good care

Advance care planning starts with an honest talk between you and your doctors. You don’t have to know the exact details of your prognosis. Just having a general idea will help with planning. With this information, you can decide at what point you will want to stop chemotherapy or other treatments, if at all. You can also decide what treatments you will want for symptom relief, such as surgery or medicine.

Another part of the planning involves hospice care. Hospice care does not include treatment to fight the cancer but rather to reduce symptoms caused by cancer. Hospice care may be started because you do not wish to continue treatment, because no other cancer treatment is available, or because you may be too sick for treatment.

Hospice care allows you to have the best quality of life possible. Care is given all day,
every day of the week. You can choose to have hospice care at home or at a hospice center. One study found that patients and caregivers had a better quality of life when hospice care was started early. These findings suggest that, especially late in the course of treatment, therapies to fight the cancer may cause more harm than good. Hospice care is particularly helpful in these situations.

An advance directive describes the treatment you’d want if you weren’t able to make your wishes known. It also can name a person whom you’d want to make decisions for you. It is a legal paper that your doctors have to follow. It can reveal your wishes about life-sustaining machines, such as feeding tubes. It can also include your treatment wishes if your heart or lungs were to stop working. If you already have an advance directive, it may need to be updated to be legally valid.

Key points

- Cervical cancer is most often diagnosed by cervical biopsy. Samples of cervical tissue are removed and tested for dysplasia and cancer.
- A cone biopsy may be used to gather more information after a cervical biopsy or to treat early cervical cancer. It involves removing a cone-shaped portion of the cervix.
- Blood tests provide helpful information about your general health and the health of your liver, kidneys, and other organs before treatment.
- Imaging helps determine the extent of the cancer before treatment. Initial imaging may include CT, MRI, PET, and/or transvaginal ultrasound.
- A cystoscopy and/or proctoscopy under anesthesia may be needed to look for signs of cancer in the bladder and bowel.
- Fertility-sparing treatment may be an option for cancer that is only in the cervix.
- The stage is a rating of the extent of the cancer before any treatment is given. It is used to determine your treatment options.
- The FIGO system is used to stage cervical cancer.
- Quitting smoking can lead to better cancer treatment outcomes. Help is available if you are ready to stop smoking.
Types of treatment

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In this chapter, the main treatments for cervical cancer are described. Your treatment options will depend on the extent of the cancer and other factors.

Surgery

Surgery is often the primary (main) treatment for early-stage cervical cancer. The types of surgery that may be used are described below.

Removing only a portion of the cervix may be an option for the earliest stage of cervical cancer. In most cases, however, the entire cervix must be removed. While this can sometimes be performed through the vagina (vaginally), an abdominal incision (cut) is usually needed. When the surgery is performed through a traditional (big) incision through the abdomen, the approach is known as laparotomy.

Minimally invasive (also called laparoscopic) surgery involves making only a few small cuts into your body. There is usually less pain and scarring compared to surgery that uses a larger cut through the abdomen. The time it takes to recover is also usually shorter.

Cone biopsy

Cone biopsy involves removing a cone-shaped section of the cervix that includes tissue from both the ectocervix and endocervix. It is a recommended treatment option for some small cervical cancers. See Part 2: Testing and staging for more information on cone biopsy.

Trachelectomy

Trachelectomy is surgery to remove the cervix. The upper part of the vagina and pelvic lymph nodes may also be removed. Trachelectomy is a fertility-sparing surgery. The uterus and ovaries are left intact, allowing for the possibility of natural pregnancy in the future.

In a simple trachelectomy, only the cervix is removed. In a radical trachelectomy, about a half inch or less of vaginal tissue is removed in addition to the cervix. Both types can be performed either through the vagina or the abdomen.

Hysterectomy

Hysterectomy is surgery to remove the uterus (including the cervix). The types of hysterectomy that may be used to treat cervical cancer are described below.

An extrafascial (simple) hysterectomy removes only the uterus (including the cervix). Extrafascial hysterectomy can be performed through the vagina, through the abdomen, or using a minimally invasive approach. This type is most commonly used for stage IA1 cancer.

A modified radical hysterectomy removes the uterus (including the cervix), a portion of the connective tissue that holds the cervix in place, and about a half inch or less of the vagina. Modified radical hysterectomy is performed through the abdomen. This type is most often used for stage IA2 cancer and higher-risk stage IA1 cancers.

A radical hysterectomy removes the uterus (including the cervix), much of the connective tissue that holds the cervix in place, and the top quarter or third of the vagina. Radical hysterectomy is performed through the
abdomen. This type is most commonly used for stages IB1 and IB2. It may be used for some stage IB3 and IIA1 cancers.

There are other differences between these hysterectomy types. If surgery is planned, your surgeon will explain the procedure recommended for you in detail.

**Ovary preservation**

The ovaries may or may not be removed during hysterectomy. If you have not entered menopause, surgery that removes both ovaries will cause menopause. This is referred to as surgical menopause. It is caused by the sudden drop in estrogen in the body. There are short- and long-term symptoms and risks of surgical menopause that can greatly affect quality of life. When caused by surgery, the symptoms of menopause may be sudden and more severe.

Symptoms include hot flashes, sleeping problems, night sweats, weight gain, and changes in mood. Vaginal atrophy is another common symptom. Vaginal atrophy is a condition in which the lining of the vagina becomes thin, dry, and inflamed. Long-term risks of not having enough estrogen include cardiovascular disease and bone loss (osteoporosis).

If hysterectomy is being considered, ask your doctor if keeping your ovaries is appropriate.

**Lymph node dissection**

Cancer cells can travel through blood and lymph. Lymph is a clear fluid that carries infection-fighting white blood cells. Lymph nodes are bean-shaped glands found throughout the body. They contain immune cells that help the body fight infection and disease.

During surgery for cervical cancer, lymph nodes may be removed in order to be tested for cancer. This is called lymph node dissection or lymphadenectomy.

In order to identify and remove the lymph node(s) most likely to contain cancer, a **sentinel lymph node biopsy** may be performed. This involves injecting a special dye or a radioactive substance into the cervix near the cancer. Lymph nodes containing the dye or substance can be seen using a special camera. These are the sentinel nodes. They are removed and tested for cancer.

Testing the removed nodes helps determine the extent (spread) of the cancer. Removing lymph nodes can also help limit the spread of cancer cells through lymph. The closest lymph nodes to the cervix are the pelvic nodes. Cervical cancer generally spreads to these nodes first. Lymph nodes in the abdomen, called the para-aortic nodes, are also sometimes removed.

**Pre-treatment surgical staging**

If the cancer has spread beyond the cervix, a hysterectomy is not performed but pelvic and/or para-aortic lymph nodes may be removed and tested before any treatment is given. Knowing whether pelvic or para-aortic nodes contain cancer can help guide treatment decisions for more advanced cancers. A minimally invasive approach is typically used to access and remove the lymph nodes. This is referred to as laparoscopic surgical staging.
Radiation therapy

Radiation therapy uses high-energy waves similar to x-rays to kill cancer cells. The two main types of radiation therapy used to treat cervical cancer are external beam radiation therapy (EBRT) and internal radiation therapy (brachytherapy).

**EBRT**

In EBRT, a large machine aims radiation at the cancer site. The radiation passes through skin and other tissue to reach the tumor and nearby lymph nodes. EBRT is given in small doses, called fractions.

An advanced type of EBRT called intensity-modulated radiation therapy (IMRT) is now commonly used to treat cervical cancer. IMRT uses many small beams of different intensities (strengths). This allows a high dose of radiation to be targeted at the tumor while limiting the amount of radiation to the surrounding normal tissue. With IMRT it is possible to reduce radiation to important nearby organs and structures, such as the bowel, bladder, external genitalia, and hip joints. This can help reduce treatment-related side effects.

Stereotactic body radiation therapy (SBRT) is a highly specialized type of external radiation therapy. It may be used to treat metastatic cervical cancer. High doses of radiation are delivered to tumors in the liver, lungs, or bone using very precise beams. Treatment is typically delivered in 5 or fewer sessions.

IMRT and SBRT are not considered brachytherapy.

**What to expect**

A planning session, called simulation, is needed before EBRT begins. You will first be...
Types of treatment

Radiation therapy

placed in the treatment position. You will be asked to lie on your back and stay very still. You may get fitted for a prop to help you stay still during the radiation sessions.

Pictures of the cancer site(s) will be obtained with a CT scan. Using the CT images and sophisticated computer software, your radiation oncologist will devise a treatment plan to aim radiation beams at the tumor and nearby lymph nodes. The plan will specify the radiation dose(s) and the number of sessions you will need. There will be several days between the time of simulation and the beginning of your treatment sessions. This allows sufficient time for careful treatment planning, dose calculation, and quality assurance.

During treatment, you will lie on a table as you did for simulation. Devices may be used to keep you from moving. This helps to target the tumor. Ink marks (tattoos) on your skin will help position your body accurately for daily treatments. You will be alone in the treatment room, but you will be able to see, hear, and speak with a technician at all times. The technician will be operating the machine from an adjacent room.

You will not see, hear, or feel the radiation being given. One session can take less than 10 minutes.

Side effects

Common side effects at the treatment site during the 5 to 6 weeks of EBRT include skin irritation, tenderness, and redness. Other short-term side effects of radiation therapy include fatigue, diarrhea, frequent or painful urination, and nausea. Most of these decrease over time when treatment is over.

Radiation therapy side effects may not be felt immediately. They may appear and worsen later in the cycle or even after it is complete.

Radiation therapy for cervical cancer can also have long-term and potentially serious side effects on fertility, sexual health, and bowel and bladder function. Radiation-induced premature menopause results when the ovaries are included in the radiation field, with symptoms similar to those of surgical menopause, as described above. See Part 6: Survivorship for information on ways to help prevent, limit, or manage these effects.

Ovarian transposition is a surgery that moves one or both ovaries out of the range of the radiation beam. The medical name for this procedure is oophoropexy. Ovarian transposition before starting EBRT may be an option if you are premenopausal and have the most common type of cervical cancer, squamous cell carcinoma. Otherwise, your doctor may consider the use of hormone replacement therapy after radiation therapy has completed. Hormone replacement therapy can help lessen some of the side effects of radiation-induced premature menopause, as discussed further in Part 6: Survivorship.

Chemoradiation

EBRT and chemotherapy (described on page 41) are often used together to treat cervical cancer. They are given concurrently (during the same time period) in a treatment strategy called chemoradiation. Chemoradiation is recommended for most locally advanced cervical cancers. These cancers have grown beyond the cervix but have not spread to the liver, lungs, or bones.
As part of chemoradiation, there are typically 5 EBRT treatment sessions per week for 5 to 6 weeks. Chemotherapy is typically given once weekly during this time. More information on chemotherapy is provided on page 41.

**Brachytherapy**

Also known as internal radiation therapy, brachytherapy involves treatment with radioactive material placed inside the body. Brachytherapy allows a high dose of radiation to be targeted at the tumor while limiting the amount delivered to surrounding normal tissue.

The radioactive material may be placed in a nearby passage or cavity, such as the vagina, endocervical canal, or endometrial cavity. This method is known as intracavitary brachytherapy. Or, the radioactive material may be placed in the tumor itself (interstitial brachytherapy). For the treatment of cervical cancer, intracavitary brachytherapy is most commonly used.

Brachytherapy for cervical cancer may be given in short bursts, called high dose-rate (HDR) brachytherapy, or in long bursts, called low dose-rate (LDR) brachytherapy. Most centers currently use HDR brachytherapy. Treatment is typically given in 3 to 5 sessions over 2 weeks.

In patients who have not had a hysterectomy, a device called an applicator is inserted into the uterus through the vagina. A “tandem and ring” applicator is commonly used for HDR brachytherapy. The tandem is a long, thin metal tube that extends into the uterus. The ring is a hollow circle that stays in the vagina, pressed against the cervix. A tandem

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**Brachytherapy**

Brachytherapy allows a high dose of radiation to be targeted at the tumor while limiting the amount delivered to surrounding normal tissue. A “tandem and ovoid” applicator is shown here.

Credit: Cancer Research UK, CC BY-SA 4.0 <https://creativecommons.org/licenses/by-sa/4.0>, via Wikimedia Commons.
and ovoid applicator uses hollow, rounded capsules instead of a ring.

General anesthesia is often required, especially for the first applicator placement. In patients without a uterus, a type of applicator called a vaginal cylinder is used. It does not extend past the vagina. General anesthesia is usually not needed when a vaginal cylinder is used.

The applicator is placed to align with the tissue targeted for treatment. Often, an imaging technique (MRI or CT) is used to guide placement of the applicator. These images are used to design the brachytherapy treatment plan. The applicator is connected to a brachytherapy machine. A radiation source travels from the machine through the hollow tubes and into the applicator. Treatment takes about 10 minutes.

If you have 2 treatment sessions in one day, or more than one session over the course of 2 days, the applicator may be left in place between treatments. This can be uncomfortable and may make it difficult to sleep.

Brachytherapy is typically started after EBRT. Shrinking the tumor with EBRT first allows for better placement of the brachytherapy applicators. Treatment with both types of radiation therapy can be completed within 8 weeks.

In some cases interstitial brachytherapy is used instead of intracavitary brachytherapy. This method involves placing needles directly into the tumor. Interstitial brachytherapy is a specialized technique that is best performed at cancer centers with experience in this method.

Side effects
The side effects of brachytherapy are similar to those of EBRT and include:

- Skin irritation near treatment area
- Tiredness (fatigue)
- Soreness in your pelvic area
- Difficulty urinating or painful urination
- Softer bowel movements or diarrhea
- Increased vaginal discharge
Types of treatment

Systemic therapy

Systemic therapy is treatment with substances that travel in the bloodstream, reaching and affecting cells throughout the body. Chemotherapy, targeted therapy, and immunotherapy are types of systemic therapy.

Most systemic therapies are given intravenously. This means they are slowly infused into your bloodstream through a vein. Infusions are often given in cycles of treatment days followed by days of rest. This allows your body to recover before the next cycle.

Chemotherapy

Chemotherapy is the most commonly used systemic therapy for cervical cancer. It stops the growth of cancer cells, either by killing the cells or by stopping them from dividing. Chemotherapy medicines that contain platinum have been found to work well against cervical cancer. The preferred platinum chemotherapy drug for cervical cancer is cisplatin.

Cisplatin is preferred, regardless of whether chemotherapy is given alone or as part of chemoradiation. If cisplatin is expected to be too harsh or cannot be given for other reasons, a different platinum drug called carboplatin is often used instead. As part of treatment with chemoradiation, cisplatin is typically given on a 7-day cycle (once weekly) for 5 to 6 weeks. When used for recurrent or metastatic cancer, infusions are typically given once every 3 weeks.

After receiving chemotherapy with cisplatin, it may not work as well again on its own if further treatment is needed. In this case, it is often given with one or two other systemic therapies, as part of a combination regimen.

Targeted therapy and immunotherapy

Targeted therapy and immunotherapy are newer types of systemic therapy. They may be options for treating cervical cancer that returns or spreads after treatment with chemotherapy. Unlike chemotherapy, targeted therapy and immunotherapy are most effective at treating cancers with specific features, called biomarkers.

Biomarkers can include proteins made in response to the cancer and changes (mutations) in the DNA of the cancer cells. Biomarker testing is used to learn whether your cancer has any targetable changes to help guide your treatment. If it does, targeted therapy or immunotherapy may be a treatment option if needed. The results of biomarker testing can also be used to determine whether you meet the criteria for joining certain clinical trials.

Testing for biomarker mutations involves analyzing a piece of tumor tissue in a laboratory or testing a sample of blood. Other names for biomarker testing include molecular testing, tumor profiling, genomic testing, tumor gene testing, next-generation sequencing, and mutation testing.

Biomarker testing is most often performed if cancer returns or spreads, but may be ordered earlier in the course of treatment.

PD-L1

Testing for this biomarker is recommended for everyone with recurrent, progressive, or metastatic cervical cancer. This is not a blood test. Testing must be done on a biopsy specimen of your tumor.
T cells are a type of white blood cell. They attack harmful things in your body, like bacteria, viruses, and cancer cells. T cells have a protein on their surface called PD-1. Cancer cells have a different protein on their surface called PD-L1. When PD-1 and PD-L1 meet, it results in an immune checkpoint. The T cell is “told” to leave the cancer alone instead of attack it.

Immunotherapy drugs known as immune checkpoint inhibitors are designed to stop these two proteins from meeting. If successful, the T cells do their job and attack the cancer cells.

A PD-L1 test measures how much PD-L1 a tumor makes. If it makes above a certain amount, the cancer is considered PD-L1 “positive.” If needed, treatment with an immune checkpoint inhibitor may be helpful for PD-L1–positive tumors.

Less common biomarkers
The biomarkers described below are less common in cervical cancer. Your doctor may test for these biomarkers if the cancer returns and/or metastasizes after initial treatment. These tests are also performed on biopsy specimens.

In normal cells, a process called mismatch repair (MMR) fixes damaged DNA. If a cell’s MMR system is not working properly, errors build up and cause the DNA to become unstable. This is known as microsatellite instability (MSI). There are two kinds of laboratory tests for this biomarker. Depending on the method used, an abnormal result is called either mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H).

The total number of mutations (changes) found in the DNA of cancer cells is known as the tumor mutational burden (TMB). If the number of mutations is higher than a specific threshold, the tumor is referred to as TMB-high (TMB-H).

In a tumor with a neurotrophic receptor kinase (NTRK) gene fusion, a piece of the NTRK gene and a piece of another gene fuse, or join. This activates the NTRK gene in a way that causes uncontrolled cell growth. NTRK gene fusion testing may be ordered for patients with a cervical sarcoma.

Side effects of systemic therapy
Systemic therapy can kill healthy cells in addition to cancer cells. The damage to healthy cells causes potentially harsh side effects. The side effects of chemotherapy depend on many factors, including the drug(s), the dose, and the person. In general, side effects are caused by the death of fast-growing cells, which are found in the intestines, mouth, and blood. As a result, common side effects include:

- Loss of appetite
- Nausea
- Vomiting
- Mouth sores
- Hair loss
- Fatigue
- Low blood cell counts (cytopenia)
- Increased risk of infection
- Bleeding or bruising easily
- Nerve damage (neuropathy)
Cisplatin can damage the kidneys. People whose kidneys do not work well may not be able to have cisplatin. An alternative chemotherapy drug may be used. Cisplatin can also cause hearing problems or loss.

Ask your treatment team for a list of common and rare side effects of each systemic therapy you are receiving. There are ways to prevent or alleviate some of these effects.

For more information on the side effects of immune checkpoint inhibitors, see the NCCN Guidelines for Patients: Immunotherapy Side Effects for Immune Checkpoint Inhibitors at NCCN.org/patientguidelines.

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**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
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 I** trials study the 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 II** trials study how well the drug or approach works against a specific type of cancer.
- **Phase III** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV** 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 with family, friends, or others whom 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. 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.

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

- Hysterectomy is surgery that removes the uterus (including the cervix). Depending on the type of hysterectomy, some of the vagina and some of the cervical connective tissue may also be removed.
- The ovaries may be removed or preserved during hysterectomy. Removing them causes surgical menopause.
- Trachelectomy is surgery that removes the cervix. It is a type of fertility-sparing surgery. The upper part of the vagina may also be removed.
- EBRT and brachytherapy are types of radiation therapy often used to treat cervical cancer.
- Chemotherapy, targeted therapy, and immunotherapy are types of systemic therapy. Platinum-based chemotherapy is the most commonly used systemic therapy for cervical cancer.
- EBRT and platinum-based chemotherapy given concurrently (during the same time period) is a treatment strategy called chemoradiation.
- Chemotherapy, targeted therapy, and immunotherapy may be options for patients with advanced, recurrent, or metastatic cervical cancer.
- Biomarker testing is used to learn whether your cancer has any targetable features. If it does, targeted therapy or immunotherapy may be a treatment option if needed.
- PD-L1 expression is the most common biomarker used to guide treatment for recurrent, worsening, or metastatic cervical cancer.
- Clinical trials give people access to investigational tests and treatments that may, in time, be approved by the FDA.
4

Treatment for common types

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60 Key points
This chapter presents recommended treatment options for the most common types of cervical cancer. While surgery is usually recommended for early-stage cancers, most locally advanced cancers are treated with chemoradiation.

The information in this section applies to the following types of cervical cancer:

- Squamous cell carcinoma
- Adenocarcinoma
- Adenosquamous carcinoma

Treatment is based on the cancer stage. The stage describes how far the cancer has likely spread based on imaging and other initial testing.

Early-stage cancer

The treatment options described in this section apply to:

- Cancers that are only in the cervix (stage I)
- Cancers that have spread to the upper vagina (stage IIA)

Surgery is recommended for most early-stage cancers. Treatment with external beam radiation therapy (EBRT) alone or chemoradiation may be recommended after surgery. If you decline or cannot have surgery, radiation therapy is usually given instead.

Surgical treatment for early-stage cervical cancer often involves surgery that removes the uterus (hysterectomy). Carrying a pregnancy is not possible after a hysterectomy. If the cancer has not spread beyond the cervix (stage I), fertility-sparing treatment may be an option if desired. Fertility-sparing treatment involves surgery that does not remove the uterus or ovaries, allowing for the possibility of natural pregnancy in the future.

A fertility-sparing approach is not appropriate for some uncommon types of cervical cancer. If fertility-sparing treatment is being considered, talk to your doctor about getting the opinion of a reproductive endocrinologist. Reproductive endocrinologists are doctors that specialize in fertility.

Options for both fertility-sparing and non–fertility-sparing treatment are provided below according to stage.
For stage IA cancers, a risk factor called lymphovascular space invasion (LVSI) plays a role in determining treatment. LVSI refers to whether there are tumor cells in the blood vessels or lymph vessels inside the tumor. If present, it means that the cancer is more likely to have spread to nearby lymph nodes. Lymph node removal is likely to be included in your treatment. Cancers with LVSI are referred to as “high-risk” below.

**Stage IA1**
Stage IA1 cancers are 3 mm or smaller. These cancers are typically diagnosed by cone biopsy. Further management depends on the presence of cancer at the margins (edges) of the removed tissue and the presence of the high-risk factor, LVSI.

If the cone biopsy results are good (no cancer in the margins and no LVSI), you may or may not have more treatment. If future fertility is not desired, an extrafascial (simple) hysterectomy is usually recommended. If fertility is desired, observation is often appropriate. Surveillance will begin (see page 53).

If the cone biopsy finds cancerous or pre-cancerous cells at the margins, there are two possibilities. Your doctor may recommend another cone biopsy to evaluate the true extent of the cancer (whether it is actually stage IA1). Otherwise, either an extrafascial (simple) hysterectomy or a modified radical hysterectomy is recommended. Lymph nodes in the pelvis may be removed during either type of hysterectomy. See page 51 for information on treatment after surgery.

**Fertility-sparing treatment**
As mentioned above, cone biopsy is the recommended fertility-sparing treatment for stage IA1 cancers. If the results are good, no further treatment is needed. If the results suggest that the cancer was not completely removed, you may have another cone biopsy. Or, your doctor may recommend radical trachelectomy.

**Stage IA2**
Stage IA2 cancers are between 3 and 5 mm. Modified radical hysterectomy and pelvic lymph node evaluation is recommended. This is also the recommended treatment for smaller (stage IA1), high-risk cancers.

If you cannot or choose not to have surgery, radiation therapy is recommended. Treatment should include both EBRT to the pelvis and brachytherapy. If the cancer is considered higher risk, platinum chemotherapy may be given concurrently with EBRT as part of chemoradiation.

**Fertility-sparing treatment**
Treatment with either cone biopsy or radical trachelectomy is recommended. Pelvic lymph node evaluation should also be performed. These options are also recommended for smaller (stage IA1), high-risk cancers. If trachelectomy is planned, see page 51 for information on treatment after surgery.

**Stages IB1, IB2, and IIA1**
Stage IB1 cancers are between 5 mm and 2 cm. Stage IB2 cancers are between 2 cm and 4 cm. Stage IIA1 cancers are 4 cm or smaller and have grown into the upper vagina.

Radical hysterectomy with pelvic lymph node evaluation is recommended for these cancers. Lymph nodes in the abdomen (para-aortic nodes) may be removed in addition to pelvic
## Treatment for early and locally advanced cervical cancer

### Guide 1

#### Treatment for common types

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<tr>
<td>• IB2</td>
<td>• IIA1</td>
<td></td>
</tr>
</tbody>
</table>
| • Radical hysterectomy and pelvic lymph node evaluation*  
• Para-aortic lymph nodes may also be removed  | Surgery (radical trachelectomy) may be an option for some stage IB2 cancers, but there is a lack of research. |
| IB3               | • IIA2                                 |                                    |
| • Radical hysterectomy and pelvic lymph node evaluation. Para-aortic lymph nodes may also be removed.  
OR  
• Chemoradiation and brachytherapy |                                    |
| • IIB             | • III                                  |                                    |
| • IVA             | • Chemoradiation and brachytherapy      |                                    |

*If you cannot or choose not to have surgery, treatment with EBRT (with or without chemotherapy) and brachytherapy is recommended.
lymph nodes. See page 51 for information on treatment after surgery.

If you cannot or choose not to have surgery, radiation therapy is recommended. Treatment should include both EBRT to the pelvis and brachytherapy. Platinum chemotherapy may be given concurrently with EBRT as part of chemoradiation.

**Fertility-sparing treatment**

Fertility-sparing treatment for stage IB1 cancer involves radical trachelectomy with pelvic lymph node evaluation. Lymph nodes in the abdomen (para-aortic nodes) may be removed in addition to pelvic lymph nodes. See the next page for information on treatment after surgery.

Radical trachelectomy with lymph node dissection may be an option for some stage IB2 cancers. However, most research on fertility-sparing surgery applies to tumors smaller than 2 cm.

**Stage IB3 and IIA2**

Stage IB3 cancers are larger than 4 cm but do not extend beyond the cervix. Stage IIA2 cancers are larger than 4 cm and have grown into the upper vagina.

These cancers may be treated as early-stage (with surgery) or as locally advanced (with chemoradiation). Currently, treatment with chemoradiation is preferred. See the next section, “Locally advanced cancer” for more information on this option.

If surgery is planned, radical hysterectomy and pelvic lymph node dissection is recommended. Lymph nodes in the abdomen (para-aortic nodes) may also be removed. See the next page for information on treatment after surgery.
Treatment after surgery
After surgery, the pathologic (surgical) stage of the cancer is determined by examining the removed tissue. The following information on treatment after surgery applies to the stages below, as determined by surgery:

- Stage I
- Stage IIA

No spread beyond the cervix
If testing finds no cancer in tissue beyond the cervix or in lymph nodes removed during surgery, there are two possibilities. Observation is recommended for cancers with no risk factors or that are not expected to benefit from radiation therapy. The other option is EBRT, which is recommended for cancers with certain risk factors.

Your doctor will consider the following when determining if EBRT is appropriate for you:

- The tumor size
- How deep the cancer extends into connective tissue
- Whether there is lymphovascular space invasion (LVSI)

If EBRT is planned, platinum chemotherapy may be given during the same time period (chemoradiation).

Cancer found in lymph nodes or tissues beyond the cervix
If cancer is found in any pelvic or para-aortic lymph nodes, or in other tissue removed with the tumor, treatment with chemoradiation is recommended. Vaginal brachytherapy may be given in addition to EBRT and platinum chemotherapy.

Next steps
Surveillance begins when treatment is complete. See page 53 for more information on surveillance testing.

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
Locally advanced cancer

This section describes treatment options for cervical cancer that has grown beyond the cervix but has not spread to the liver, lungs, or bones. Cancers that are close to spreading beyond the cervix (stage IB3) are also considered locally advanced. Locally advanced cancers are not metastatic.

The information in this section applies to the following stages:

- Stage IB3 and IIA2
- Stage IIB
- Stage III
- Stage IVA

Locally advanced cancers are more likely to have spread to lymph nodes than early-stage cancers. Knowing whether pelvic and/or para-aortic nodes contain cancer can help guide treatment with EBRT for these cancers. Additional imaging may be performed to identify cancerous lymph nodes.

Another approach is to surgically remove and test lymph nodes before any treatment is given. A minimally invasive approach is typically used to access and remove the lymph nodes. This is referred to as surgical staging. If surgical staging is performed, the para-aortic lymph nodes are typically removed. Pelvic lymph nodes may or may not be removed.

Treatment with all of the following is recommended for most locally advanced cervical cancers:

- Chemoradiation (concurrent EBRT and platinum chemotherapy)
- Brachytherapy

If cancer is present in pelvic lymph nodes, EBRT will include the pelvis. If any para-aortic nodes are known or suspected to have cancer, EBRT will be given to a larger treatment area that includes these nodes as well.

While treatment as described above is currently preferred for stage IB3 and IIA2 cancers, surgery is sometimes recommended. See page 50 for more information.

Next steps
See the next page for information on surveillance testing after treatment.
Surveillance

After finishing treatment, you will have testing to look for early signs of possible recurrence. This is known as surveillance. The surveillance testing information that follows applies to common types of cervical cancer and to small cell neuroendocrine carcinoma of the cervix (NECC).

Physical exams and health updates
Physical exams performed by your oncologist are an important part of surveillance, especially in the first 5 years after treatment. At these follow-up visits, tell your doctor about any changes in your health. Such changes include new or worsening symptoms and other health conditions or concerns.

The recommended time frames for these follow-up visits are shown in Guide 2. Time frame ranges (eg, every 3 to 6 months) are used to allow for differences in individual risk of recurrence and in patient and provider preference. Patients considered at higher risk of recurrence may benefit from more frequent exams than lower-risk patients.

After the fifth year, these visits are generally spaced out to once per year (annually). Or, you and your doctor may agree on a different schedule after discussing your individual risk of recurrence.

Imaging
Unlike physical exams, imaging is generally not needed at regular intervals for an extended time after treatment. Imaging is typically ordered if you have new or worsening symptoms, or if other findings suggest recurrence or spread. Follow-up imaging is described below according to the cancer stage.

Stage I
After non–fertility-sparing treatment, you may have a positron emission tomography/computed tomography (PET/CT scan) 3 to 6 months after finishing treatment. This follow-up imaging may be helpful for stage IB3 cancers and for patients who had treatment with radiation or chemoradiation after surgery. The area from the neck to the mid thigh is typically scanned.

After fertility-sparing treatment, you may have an MRI of your pelvis (with contrast) 6 months after surgery and then yearly for 2 to 3 years.

Stages II, III, and IVA
Follow-up imaging is recommended 3 to 6 months after finishing treatment for stage II, III, or IVA cervical cancer. A PET/CT scan is preferred, but a CT with contrast is also a recommended option. The area from the neck to the mid thigh will be scanned.

Other imaging for these stages may include a pelvic MRI with contrast 3 to 6 months after finishing treatment.

Metastatic cancer
For stage IVB or distant recurrences of cervical cancer, imaging is used mainly to learn how the cancer is responding to systemic therapy. Imaging may include CT, MRI, and/or PET/CT.

Pap tests
Depending on the type of surgery you have (if any), after treatment you may have annual Pap screening tests. Pap testing is helpful for finding new areas of abnormal and/or pre-cancerous cells. It is not as effective at
detecting recurrent cervical cancer. Pap testing is also known as cervical or vaginal cytology.

**Blood tests**
If you have symptoms, or a physical exam was suspicious for recurrence, your doctor may order blood tests. In addition to a complete blood count (CBC), testing may measure blood urea nitrogen (BUN) and creatine levels. BUN and creatine are waste products typically filtered out by the kidneys. A high level of these in the blood may be a sign of a kidney problem.

**Survivorship**
In addition to surveillance testing, a range of other care is important for cancer survivors. This includes keeping alert for symptoms of cancer recurrence. See *Part 6: Survivorship* for more information.

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**Guide 2**
**Physical exam surveillance schedule**

<table>
<thead>
<tr>
<th>Years 1 and 2 after treatment</th>
<th>Every 3 to 6 months</th>
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<tbody>
<tr>
<td>Years 3, 4, and 5 after treatment</td>
<td>Every 6 to 12 months</td>
</tr>
<tr>
<td>After the 5th year</td>
<td>Once a year or as agreed upon with your doctor</td>
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</table>
Persistence or recurrence

This section discusses cervical cancer that does not improve with treatment (persistent) or that returns after treatment (recurrent). If your doctor suspects recurrence or spread, a CT or PET/CT scan of your neck, chest, abdomen, pelvis, and groin is recommended. You may also have a pelvic MRI.

Surgery to look inside the body (exploratory surgery) may be helpful in some cases. The goal is to learn the extent of the cancer. This can help guide treatment decisions.

In order to know whether you may be eligible for a targeted therapy or immunotherapy, biomarker testing is recommended. Comprehensive genomic profiling (CGP) involves testing for many biomarkers at the same time.

If biomarker testing can be performed on a sample taken from a metastatic tumor, this method is preferred. Otherwise, a sample of blood may be tested instead. See page 41 for more information on biomarkers.

If cancer returns to the pelvis

Cervical cancer that returns to the pelvis, but not to distant areas of the body, is known as a local or regional recurrence. Treatment options depend on whether you’ve had EBRT at the cancer site.

No prior EBRT

If the cancer can be resected (surgically removed), resection is generally preferred. Otherwise, if not previously given, EBRT is recommended to treat cervical cancer that returns to the pelvis. EBRT may also be an option if you had external radiation in the past, but not at the site of new cancer growth. Systemic therapy and/or brachytherapy may be given in addition to EBRT.

Prior treatment with EBRT

If further treatment with EBRT is not possible and the cancer is very small (2 cm or less), radical hysterectomy or brachytherapy may be treatment options. These treatments are typically only considered in carefully selected patients. Otherwise, pelvic exenteration (described next) is considered.

Pelvic exenteration

Pelvic exenteration is a radical surgery that involves removing multiple organs from the pelvis. The goal is to cure the cancer by removing all of the organs to which cancer has or may spread.

All remaining organs of the female reproductive system are removed during pelvic exenteration. This includes the uterus, fallopian tubes, ovaries, and vagina. Nearby organs in the pelvis including the bladder, rectum, and/or anus may also be removed.

If the bladder and/or organs involved in bowel function are removed, a diversion is typically performed. Diversions are surgical procedures that divert (redirect) urine and/or stool to new openings through which they exit the body.

Vaginal reconstruction

It is often possible to reconstruct the vagina after pelvic exenteration. A surgeon can create an artificial vagina using muscle from another area of your body. A muscle in the lower abdomen called the rectus abdominus is often used for vaginal reconstruction. This procedure is sometimes referred to as muscle flap reconstruction.
If the bladder is removed
An ileal (incontinent) conduit is one type of urinary diversion. After the bladder is removed, your surgeon will create a new tube from a piece of intestine (ileum). This tube will allow your kidneys to drain. Your urine will now exit the body through a small opening called a stoma. A small disposable bag attached to the outside of your abdomen collects the urine. This is called an ostomy bag or ostomy pouch. The bag stays attached to your body with the help of an adhesive part called a “wafer.” The wafer sticks to the skin and acts as a watertight barrier.

Another way urine may be redirected after removing the bladder is a continent urinary diversion. It is also referred to as an artificial bladder or “Indiana pouch.” This method uses a segment of intestine to create a pouch to hold urine. The pouch has a channel for urine to pass through made from intestine that connects it to the wall of the abdomen.

A stoma is made in the abdominal wall at the location of the reservoir. Sometimes the stoma can be made in the belly button, making it less noticeable. To drain urine, a catheter is inserted into the reservoir several times a day. A benefit to this type of urinary diversion is that an ostomy bag does not need to be worn on the outside of the body.

If the rectum is removed
If the rectum is removed, a permanent colostomy may be created. A colostomy connects the remaining colon to the outside of the abdomen. Stool exits the body through a stoma and goes into a bag attached to the skin. In some cases, the remaining colon can be connected to the remaining rectum or anus and a permanent colostomy may not be required. You may retain near-normal bowel function. If the anus is removed during the surgery, a permanent colostomy is always needed.

If both the bowel and bladder are removed
If both urinary and fecal diversion are needed, a double-barreled wet colostomy (DBWC) is sometimes used. In this technique, only one opening (stoma) on the surface of the abdomen is needed. Urine and stool are kept separate until they exit the body through the same stoma. Compared to having separate urinary and fecal diversions, DBWC has been found to have other benefits, such as fewer leaks.

Distant recurrence
If cancer returns after treatment and is found in other areas of the body, such as the liver or lungs, it is known as a distant recurrence. The cancer is metastatic. The new cancer growths, or tumors, are called metastases. See “Metastatic cancer” on the next page for information.
Metastatic cancer

If left untreated, cervical cancer often spreads to the liver, lungs, and/or bone. Cervical cancer that has spread to these organs is metastatic. Cancer that had already metastasized when it was found is stage IVB. If cancer returns and metastasizes after treatment, it is known as a distant recurrence. The information in this section applies to both types of metastatic disease.

Metastatic cervical cancer is very hard to cure. Treatment is usually with systemic therapy. The goal is to keep the cancer under control and prevent further spread. If the tumor has not already been tested for certain biomarkers, including tumor mutational burden (TMB), it may be tested now. Biomarker testing can help determine whether you may be eligible for certain targeted therapies or immunotherapies.

In some cases, it may be possible to remove or destroy the new cancer growth(s) using local therapies. Local therapies are treatments

Hypersensitivity reactions

With repeat use of cisplatin or carboplatin, you are at an increased risk of having a hypersensitivity reaction (also called an allergic reaction) that could be life-threatening. If your treatment team hasn’t brought it up, below are some questions you can ask to get more information about this risk.

- How likely is it that I will have an allergic reaction to chemotherapy?
- How will I know if I’m having an allergic reaction? What are the symptoms?
- Does the staff on hand have the expertise and equipment to manage hypersensitivity reactions?
that target tumors directly. Surgery (resection), EBRT, and ablative therapies are local therapies. Treatment strategies that involve local therapies include:

- Resection with or without EBRT
- Local ablative therapies with or without EBRT
- EBRT with or without systemic therapy

Ablative therapies destroy cancerous lesions with little harm to nearby tissue. They are often delivered using a specially designed needle (a probe or electrode) placed directly into or next to the tumor.

Stereotactic body radiation therapy (SBRT) is a highly specialized type of EBRT that may be used to treat tumors in the liver, lungs, or bone. Treatment is performed in only a few sessions.

When treatment with local therapies is complete, your doctor may recommend systemic therapy. After finishing treatment, surveillance begins or resumes.

**Systemic therapy**
Metastatic cervical cancer is most commonly treated with systemic therapy. If you have not yet received platinum-based chemotherapy, you are likely to receive it now. If you had prior treatment with cisplatin, it may not work as well again on its own. In this case, it is often given with one or two other systemic therapies, as part of a combination regimen.

A factor your doctor will consider when selecting a combination systemic therapy regimen to use first (as “first-line” therapy) is whether the cancer has the PD-L1 biomarker.

At this time, the preferred first-line combination regimen for **PD-L1 positive cancers** is pembrolizumab (Keytruda®) with cisplatin and paclitaxel (a different type of chemotherapy). Bevacizumab (Avastin®) may also be included. Pembrolizumab is an immune checkpoint inhibitor (a type of immunotherapy). Bevacizumab is a type of targeted therapy called a biologic that is designed to work with chemotherapy.

The preferred first-line combination regimen for all other metastatic cervical cancers is cisplatin with paclitaxel and bevacizumab.

Other recommended first-line regimens include different combinations of cisplatin (or carboplatin), topotecan, paclitaxel, and/or bevacizumab.

**Second-line or later systemic therapy**
If you cannot have more platinum-based chemotherapy, there are other options for chemotherapy that do not contain platinum. Or, if the cancer has certain biomarkers (features), treatment with immunotherapy or targeted therapy may be an option. Biomarkers and their related systemic therapies are listed in Guide 3. See page 41 for more information on biomarkers.

If treatment with an immune checkpoint inhibitor is planned, see the NCCN Guidelines for Patients for Immunotherapy Side Effects: Immune Checkpoint Inhibitors at NCCN.org/patientguidelines.
Supportive care
Supportive care is available to everyone with metastatic cervical cancer, regardless of whether you are in active treatment. Supportive care refers to a range of care and resources often needed by patients with metastatic cancer. Hospice care, access to pain specialists, and emotional and spiritual support are all components of supportive care. Because metastatic cancer cannot be cured, the main goal of supportive care is to make you more comfortable and to help keep the cancer under control. Supportive care may also help you live longer and feel better overall. When used for advanced cancers, supportive care is often called palliative care.

You may also consider enrolling in a clinical trial. A clinical trial is a type of research study that involves people. Ask your treatment team if there is an open clinical trial that you can join. Clinical trials are discussed in more detail at the end of Part 3: Types of treatment.

Guide 3
Biomarkers and their related therapies

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<tr>
<td>PD-L1 positive</td>
<td>• Pembrolizumab (Keytruda®)</td>
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<td></td>
<td>• Nivolumab (Opdivo®)</td>
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<tr>
<td>Mismatch repair deficient/microsatellite</td>
<td>Pembrolizumab (Keytruda®)</td>
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<td>instability-high (dMMR/MSI-H)</td>
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<tr>
<td>Tumor mutational burden-high (TMB-H)</td>
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<tr>
<td>NTRK gene fusion positive</td>
<td>• Larotrectinib (Vitrakvi®)</td>
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<tr>
<td></td>
<td>• Entrectinib (Rozlytrek®)</td>
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Key points

Early-stage and locally advanced

- Treatment for early-stage cervical cancer often involves surgery to remove the uterus (hysterectomy). If you cannot or choose not to have surgery, treatment with EBRT and brachytherapy is recommended.
- Treatment with EBRT alone or chemoradiation may be recommended after surgery for early-stage cancer.
- Fertility-sparing treatment may be an option for some stage I cancers. Treatment typically involves either cone biopsy or radical trachelectomy.
- Extra imaging and/or surgical staging may be performed for locally advanced cancers in order to learn about spread to lymph nodes.
- Combined treatment with chemoradiation and brachytherapy is recommended for most locally advanced cervical cancers.

Surveillance

- Surveillance after cervical cancer treatment involves periodic physical exams and staying alert for symptoms of recurrence or spread.
- Follow-up imaging with CT or PET/CT is recommended 3 to 6 months after finishing treatment for stage II, III, or IVA cancer. A pelvic MRI with contrast may also be ordered.
- Imaging is generally not needed on an ongoing basis to check for recurrence. Scans are typically ordered if you have symptoms or if your doctor suspects recurrence for other reasons.

Recurrence

- If you have never had treatment with EBRT, it is likely to be used to treat cancer that returns to the pelvis.
- Pelvic exenteration surgery may be used to treat cervical cancer that returns to the pelvis and cannot be treated with radiation therapy.

Metastatic cancer

- Metastatic cervical cancer is usually treated with systemic therapy. Platinum-based chemotherapy is recommended when possible.
- If the cancer has specific biomarkers, you may be eligible for treatment with a targeted therapy or immunotherapy.
- It may be possible to remove or destroy new cancer growth(s) using local therapies such as resection, EBRT, and ablative treatments.
- Supportive care is available to everyone with cervical cancer.
5
Treatment for neuroendocrine carcinoma of the cervix (NECC)

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This chapter presents treatment options for a rare type of cervical cancer called neuroendocrine carcinoma of the cervix (NECC). Treatment often involves chemotherapy and both external and internal radiation therapy. Surgery may be an option for small cancers.

There is more than one subtype of NECC. The most common is small cell. Treatment for small cell NECC is the focus of this section.

Treatment for NECC often involves chemotherapy, alone or as part of chemoradiation. The combination of cisplatin and a different chemotherapy drug called etoposide is preferred for chemotherapy, whether it is given alone or with external beam radiation therapy (EBRT). If you cannot have cisplatin, carboplatin is often substituted.

NECC tumors can contain cells from more common types of cervical cancer, including squamous cell carcinoma. If a cancer contains both NECC cells and cells from a more common type, the cancer is treated as NECC.

See Part 3: Types of treatment for more information on the treatments discussed in this section.

Early-stage cancer

For cancers that have not spread beyond the cervix, treatment is guided by the size of the tumor.

Tumors 4 cm or smaller
If you are a candidate for surgery, radical hysterectomy and pelvic lymph node dissection is recommended for tumors 4 cm or smaller. Para-aortic lymph nodes may or may not be removed for testing. Treatment with either chemotherapy alone or chemoradiation (chemotherapy and EBRT) follows surgery.

A second option for tumors 4 cm or smaller is treatment with chemoradiation (chemotherapy and EBRT) and brachytherapy. When treatment is over, your doctor may recommend additional systemic therapy.

Tumors larger than 4 cm
One option for tumors 4 cm or larger is chemoradiation and brachytherapy first. More chemotherapy may follow.

Another possibility is that chemotherapy will be given first to try to shrink the cancer. If chemotherapy works well, surgery (hysterectomy) may be performed. After surgery, further treatment with EBRT alone or chemoradiation may be given. More chemotherapy may follow.

If surgery is not performed, treatment with chemoradiation (EBRT and chemotherapy) and brachytherapy is the next step. More chemotherapy may follow.
Locally advanced NECC

The term locally advanced is used to describe cervical cancer that has grown beyond the uterus but has not spread to the liver, lungs, or bone. This includes stage II, III, and IVA cancers. Cancers that are close to spreading beyond the uterus (stage IB3) are also considered locally advanced. Locally advanced cancers are non-metastatic.

Currently, combined treatment with chemoradiation (chemotherapy and EBRT) and brachytherapy is preferred for these cancers. When chemoradiation and brachytherapy are finished, you may receive additional chemotherapy with the same regimen.

The other recommended strategy is treatment with chemotherapy first, followed by chemoradiation and brachytherapy.

After initial treatment
If initial treatment works well, surveillance will begin. Surveillance involves testing to look for early signs of recurrence. The surveillance strategy for more common types of cervical cancer is also recommended for NECC. See page 53 for information. If the cancer returns and/or spreads during surveillance, see information on recurrent and/or metastatic NECC provided below.

If the cancer does not improve with initial treatment, it is known as “persistent.” Options for treating persistent NECC that is only in the pelvis may include:

- Systemic therapy
- Pelvic exenteration surgery

These are also treatment options for recurrent, non-metastatic NECC.

If the cancer spreads to the liver, lungs, or bone (metastasizes), see “Metastatic cancer” in Part 4: Treatment for common types. Recommendations for treating metastatic cancer apply to common cervical cancers and to NECC.

Supportive care
Supportive care is always an option. This care is available to everyone with persistent, recurrent, or metastatic cancer, regardless of whether you are in active treatment. Supportive care refers to a range of resources offered to patients with advanced or metastatic cancer. Hospice care, access to pain specialists, and emotional and spiritual support are all components of supportive care.

Because the cancer cannot be cured, the main goal of supportive care is to make you more comfortable and to help keep the cancer under control. Supportive care may also help you live longer and feel better overall. When used for advanced cancers, supportive care is often called palliative care.

Consider a clinical trial
Enrolling in a clinical trial allows you to receive treatment while helping researchers learn more about this rare cancer. Ask your treatment team if you are eligible for any current clinical trials. Clinical trials are discussed in more detail at the end of Part 3: Types of treatment.
Key points

➤ Small cell NECC is a rare and usually aggressive (fast-growing) type of cervical cancer.

➤ Treatment for NECC often involves chemotherapy, EBRT, and brachytherapy. Surgery (combined with other treatment) may also be an option for early-stage NECC.

➤ Options for treating persistent NECC that is only in the pelvis include systemic therapy and possibly pelvic exenteration surgery.

➤ Supportive care is an option for everyone with NECC. Talk to your treatment team about resources available to you.

➤ There is much to be learned about rare cancers like small cell NECC. Think about enrolling in a clinical trial for treatment.
Survivorship

- Staying alert for recurrence or spread
- Late and long-term effects
- Help for side effects
- Healthy habits
- More information
- Key points
Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the long-term side effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

After finishing cancer treatment, your primary care doctor, also known as a general practitioner (GP) or primary care physician (PCP), will play an important role in your care. Your oncologist (cancer doctor) and PCP should work together to make sure you get the follow-up care you need. To help do this, your oncologist should develop a written survivorship care plan that includes:

- A summary of your cancer treatment history, including surgeries, radiation treatments, and/or chemotherapy
- A description of possible short-term, late, and long-term side effects
- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your PCP
- Clear roles and responsibilities for both your cancer care team and your PCP
- Recommendations on your overall health and well-being

Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the long-term side effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

Staying alert for recurrence or spread

Your cancer treatment team and your primary care doctor will work together to make sure you get recommended follow-up testing. But, you will have one of the biggest responsibilities—paying close attention to your body. If cervical cancer does come back, it may affect your body in ways that you can feel or notice (symptoms).

Your doctor will teach you about the symptoms that may mean cervical cancer has returned or spread. They include:

- Vaginal discharge or bleeding
- Blood in your urine or stool
- Weight loss
- Loss of appetite
- Pain in the pelvis, hips, back, or legs
- Coughing
- Shortness of breath
- Swelling in your stomach or legs

If you notice any of these symptoms, contact your doctor right away. Do not wait until your next scheduled visit.
Late and long-term effects

Some side effects of cervical cancer treatment can start early and linger longer than expected, while others may not appear until long after treatment is over. Many cervical cancer survivors experience problems with bowel, urinary, and sexual function. The extent and degree of symptoms vary widely between patients. Ask your treatment team for a complete list of possible late and long-term side effects.

Physical side effects

Bowel and bladder changes
Urinary incontinence (the inability to hold urine in the bladder) and urgency (a sudden, strong need to urinate) are possible after surgery or radiation therapy for cervical cancer. Watery and/or frequent bowel movements (diarrhea) are also possible. Occasional bleeding may occur either with urination or bowel movements.

Sexual side effects
Sexual side effects can occur after cervical cancer treatment, including:

- Reduced sex drive (libido)
- Vaginal dryness
- Pain during sex
- Narrowing and shortening of the vagina (vaginal stenosis)

Infertility and premature menopause
Removing the ovaries or exposing them to radiation causes infertility. Early-onset menopause symptoms may also occur. These include cessation (stopping) of menses, hot flashes, night sweats, weight gain, and mood changes. Vaginal atrophy is another common symptom. Vaginal atrophy is a condition in which the lining of the vagina becomes thin, dry, and inflamed. Long-term risks of not having enough estrogen include cardiovascular disease and bone loss (osteoporosis).

Other physical side effects
In addition to effects on bowel, bladder, and sexual function, more general effects such as fatigue, trouble breathing (dyspnea), and difficulty sleeping (insomnia) are common.

Radiation treatment to the pelvis can weaken bones in the pelvis, putting you at increased risk of fractures. Your doctor may want to start monitoring the density of your bones.

Chemotherapy can damage the sensory nerves. This is known as neuropathy. The damage can result in pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It often begins in the hands or feet and gets worse over time. Neuropathic pain is often described as a shooting or burning pain.

Treatment for cervical cancer often involves removing lymph nodes during surgery. Lymph may not drain properly after lymph nodes are removed. This can result in lymphedema. Lymphedema is swelling caused by a build-up of lymph fluid in tissues. It most often occurs in the lower body for cervical cancer survivors.

Effects on mental health
The effects of cervical cancer and its treatment can be difficult to cope with. Many survivors report having an overall lower quality of life after cancer treatment. Depression, anxiety, fear of recurrence, and trouble adjusting
to changes in the body are possible. Many people also have financial stressors, such as concerns or hesitation about returning to work and insurance coverage issues. Personal relationships, sexuality, and intimacy may also be affected by a cancer diagnosis or cancer treatment.

Help for side effects

**Pelvic floor physical therapy**
The pelvic floor is a group of muscles that supports the organs of the pelvis. These muscles play a key role in bowel and bladder control and well as sexual function and arousal. There are ways to strengthen these muscles before and after treatment. This is known as pelvic floor physical therapy, and there are health care professionals that specialize in it. Pelvic floor therapy can include at-home exercises to tighten and release the vaginal and anal muscles (Kegel exercises) as well as hands-on techniques by a physical therapist. Ask your treatment team for help finding a pelvic floor specialist in your area.

**Hormone replacement therapy**
Due to surgical removal of the ovaries, or radiation exposure, women experience a drop in the hormones produced by the ovaries (estrogen and progesterone). When these hormonal changes result in menopausal symptoms, hormone therapy consisting of systemic combinations of estrogen (and progestins for those with a uterus intact) and vaginal applications of estrogen may help. Discussion with a menopausal symptom team is recommended to determine whether this treatment is right for you.

**Vaginal moisturizers**
Older age, menopause, and some cervical cancer treatments can cause the vagina to become dry and less stretchy. To offset this side effect, use of water-based vaginal moisturizers is highly encouraged. Like moisturizers for your body, vaginal moisturizers restore moisture to the vagina and help to keep the vaginal tissue healthy. Vaginal moisturizers can be used daily. Many come with applicators to make using them easier. Vaginal estrogen cream or tablets may be particularly helpful where there has been thinning of the vaginal and vulvar tissues due to loss of estrogen.

**Vaginal dilator therapy**
Radiation therapy to the pelvic area can cause the vagina to become shorter and narrower. This is called vaginal stenosis. Vaginal stenosis can make it uncomfortable or even painful to have sex, or to have vaginal examinations by a doctor. Vaginal dilator therapy can be used to lessen the effects of vaginal stenosis. A vaginal dilator is a device used to gradually stretch or widen the vagina. You can start using a dilator as soon as 2 to 4 weeks after radiation therapy has ended and can continue to use it for as long as you want. Vaginal dilators are not one-size-fits-all. Different sizes are available, as are dilator kits containing different size devices. The size of the dilator can be increased over time as the vagina lengthens and widens.

**Ostomy care**
If you have an ostomy, you want to join an ostomy support group. Another option is to see a health care provider that specializes in ostomy care, such as an ostomy nurse. People with ostomies can still live very active
lifestyles. Consider consulting with an ostomy professional before undertaking vigorous physical activity.

**Sexual health therapists**
While it may be uncomfortable to talk about sexual health, keep in mind that these side effects are common and can often be managed or lessened. Consider seeing a sexual health therapist. These health care professionals specialize in helping cancer survivors and others overcome and manage sexual side effects of cancer treatment. Many cancer treatment centers have programs focused solely on sexual health after cancer treatment. Ask your doctor about resources available through your cancer center that can help minimize the impact of cancer treatment on your sexual health.

**Mental health and wellness**
If you are anxious, distressed, depressed, or are just having trouble coping with life after cancer, you are not alone. Tell your treatment team about these symptoms. Expect your treatment team to ask about your mental health. If they don’t, speak up. There are many resources available that can improve mental health and wellness for cancer survivors. Social workers at your treatment center are often excellent resources to help connect you with mental health and financial resources.

**Healthy habits**
Monitoring for the return of cervical cancer is important after finishing treatment. But, it is also important to keep up with other aspects of your health. Steps you can take to help prevent other health issues and to improve your quality of life are described next.

Get screened for other types of cancer, such as breast, skin, and colorectal cancer. Talk to your primary care doctor about recommended cancer screening tests for your age and risk level.

Get other recommended health care such as blood pressure screening and hepatitis C screening, and immunizations (such as the flu shot).

Leading a healthy lifestyle includes maintaining a healthy body weight. Exercising at a moderate intensity for at least 150 minutes per week is recommended. Talk to your doctor before starting a new exercise regimen. Try to eat a healthy diet that includes lots of plant-based foods.

Radiation treatment to the pelvis can weaken bones in the pelvis, putting you at increased risk of fractures. Your doctor may want to start monitoring the density of your bones.

Alcohol may increase the risk of certain cancers. Drink little to no alcohol.

If you are a smoker, quit! Your doctor can provide (or refer you for) counseling on how to stop smoking.
More information

For more information on cancer survivorship, the following resources are available at NCCN.org/patientguidelines:

- Survivorship Care for Healthy Living
- Survivorship Care for Cancer-Related Late and Long-Term Effects

These resources address many topics relevant to cervical cancer survivors, including:

- Anxiety, depression, and distress
- Cognitive dysfunction
- Fatigue
- Pain
- Sexual health
- Sleep disorders
- Healthy lifestyles
- Immunizations
- Employment, insurance, and disability concerns

Key points

- Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors.
- Ask your oncologist (cancer doctor) about a survivorship care plan. This document can help your oncologist and PCP coordinate your follow-up care.
- It is important to stay alert for signs of potential recurrence or spread, including vaginal discharge or bleeding, blood in your urine or stool, and weight loss.
- Many cervical cancer survivors experience problems with bowel, urinary, and sexual function.
- Other physical side effects include infertility, early menopause, fatigue, trouble breathing, insomnia, painful nerve damage, and swelling of the legs.
- Pelvic floor physical therapy, hormone replacement therapy, and vaginal moisturizers and dilators can help with some side effects.
- Sexual health therapists specialize in helping cancer survivors and others overcome and manage sexual side effects of cancer treatment.
- Depression, anxiety, fear of recurrence, and trouble adjusting to changes in the body are possible after cervical cancer treatment.
- Talk to your treatment team about resources that can improve mental health and wellness for cancer survivors.
Making treatment decisions

72  It’s your choice
72  Questions to ask your doctors
77  Resources
It is important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It’s your choice

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

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 like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from 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 doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer should not be ignored, there is time to have another doctor 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 your doctors

Possible questions to ask your doctors 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. Keep a notebook handy to record answers to your questions.
Questions to ask about treatment

1. What treatment plan do you recommend for me?

2. Which treatments does it include?

3. What are the risks and benefits of each treatment? What about side effects?

4. Will my age, general health, and other factors affect my treatment options?

5. Would you help me get a second opinion?

6. How soon should I start treatment? How long does treatment take? Is there a clinical trial that I can join?

7. Where will I be treated? Will I have to stay in the hospital or can I go home after each treatment?

8. What can I do to prepare for treatment?

9. What symptoms should I look out for during treatment?

10. How much will the treatment cost? How can I find out how much my insurance company will cover?

11. How likely is it that I will be cancer-free after treatment?

12. Are there supportive services that I can get involved in? Support groups?
Questions to ask about recurrence

1. How likely is it that the cancer will return? What is my risk based on?

2. Will I need pelvic exenteration? If so, which organs will be removed?

3. Will I need an ostomy?

4. How likely is the cancer to metastasize? Where does it usually spread?

5. Am I eligible for treatment with a targeted therapy or immunotherapy?

6. What biomarkers does my cancer have?

7. What if the cancer returns a second time?
Questions to ask about clinical trials

1. Is a clinical trial right for me?
2. What is the purpose of the study?
3. How many people will be in the clinical trial?
4. What are the tests and treatments for this study? How often will they take place?
5. Has the drug been used before? Has it been used for other types of cancers?
6. What side effects can I expect? Can the side effects be controlled?
7. How long will I be in the clinical trial?
8. Will you know if the treatment is working?
9. Will I be able to get other treatment if this treatment doesn’t work?
10. Who will help me understand the costs of the clinical trial?
What is your experience?

1. Are you board-certified? If yes, in what area?

2. How many patients like me have you treated?

3. How many procedures like the one you’re suggesting have you done?

4. Is this treatment a major part of your practice?

5. How many of your patients have had complications?
Resources

American Cancer Society
cancer.org/cancer/cervical-cancer.html

CancerCare
cancercare.org

Cancer.Net
cancer.net/cancer-types/cervical-cancer

Centers for Disease Control & Prevention (CDC)
cdc.gov/cancer/cervical

Cervivor
cervivor.org

HPV Cancers Alliance
hpvalliance.org

National Cancer Institute (NCI)
cancer.gov/types/cervical

National Cervical Cancer Coalition (NCCC)
nccc-online.org

National Coalition for Cancer Survivorship
canceradvocacy.org

NCCN Reimbursement Virtual Resource
NCCN.org/reimbursement

share with us.

Take our survey
And help make the NCCN Guidelines for Patients better for everyone!
NCCN.org/patients/comments
Words to know

**abdomen**
The belly area between the chest and pelvis.

**adenocarcinoma**
Cervical cancer that starts in glandular cells in the endocervix. About 2 out of 10 cervical cancers are adenocarcinomas.

**adenosquamous carcinoma**
A less common type of cervical cancer that contains both squamous cells and gland-like cells.

**biomarkers**
Specific features of cancer cells. Biomarkers can include proteins made in response to the cancer and changes (mutations) in the DNA of cancer cells.

**biopsy**
Removal of small amounts of tissue or fluid to be tested for disease.

**blood chemistry profile**
A test that measures the amounts of many different chemicals in a sample of blood.

**brachytherapy**
A type of radiation therapy in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near a tumor. Also called internal radiation therapy.

**cancer grade**
A rating of how abnormal cancer cells look when viewed under a microscope.

**cancer stage**
A rating of the extent of cancer in the body.

**cervical intraepithelial neoplasia (CIN)**
Abnormal and potentially pre-cancerous cells on the surface of the cervix. Also called cervical dysplasia.

**cervix**
The lower part of the uterus that connects to the vagina.

**clinical trial**
A type of research involving people that assesses investigational tests or drugs.

**complete blood count (CBC)**
A common test that measures the number of white red cells, blood red cells, and platelets in a sample of blood.

**computed tomography (CT)**
An imaging test that uses x-rays from many angles to make a picture of areas inside the body.

**cone biopsy**
A procedure in which a cone-shaped piece of abnormal tissue is removed from the cervix. May be used to gather more information about the extent of a cancer or to treat some early cervical cancers.

**contrast**
A substance put into your body to make clearer pictures during imaging tests.

**ectocervix**
The rounded, outer part of the cervix that extends into the vagina. The ectocervix is lined with cells called squamous cells.

**endocervix**
The inner part of the cervix that forms a canal between the vagina and the uterus. The endocervix is lined with columnar (glandular) cells that make mucus.

**external beam radiation therapy (EBRT)**
Treatment with radiation received from a large machine outside the body. Types of EBRT include intensity-modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT).
**extrafascial hysterectomy**
Surgery to remove the uterus (including the cervix). The vagina is not removed. The connective tissue and fat surrounding the cervix is not removed. Also called simple hysterectomy.

**fallopian tube**
A thin tube through which an egg travels from the ovary to the uterus.

**gynecologic oncologist**
A surgeon who is an expert in cancers that start in the female reproductive organs.

**hot flash**
A short period of intense body heat and sweating.

**hormone**
A chemical in the body that activates cells or organs.

**human papillomavirus (HPV)**
A common sexually transmitted infection. Almost all cervical cancers are caused by long-term HPV infection.

**infusion**
A method of giving drugs slowly through a needle into a vein.

**lymph**
A clear fluid containing white blood cells that fight infection and disease.

**lymph nodes**
Small groups of disease-fighting cells located throughout the body.

**lymphovascular space invasion (LVSIs)**
The presence of tumor cells in the blood vessels or lymph vessels inside the tumor. LVSIs is a risk factor for cancer spread.

**magnetic resonance imaging (MRI)**
A type of imaging test that does not use radiation. MRI uses radio waves and powerful magnets to make pictures of areas in the body.

**medical oncologist**
A doctor who is an expert in treating cancer with systemic therapies, such as chemotherapy.

**menopause**
The point in time when menstrual periods end.

**metastasis**
The spread of cancer cells from the first tumor to another body part.

**modified radical hysterectomy**
Surgery to remove the uterus (including the cervix). A half inch or less of the vagina is also removed. Some of the connective tissue and fat surrounding the cervix is also removed.

**mutation**
A change in the DNA sequence of a cell. Mutations may be inherited, random, or caused by DNA-damaging sources in the environment. Some mutations are biomarkers (features) that may guide cancer treatment.

**neuroendocrine carcinoma of the cervix (NECC)**
A rare and often aggressive subtype of cervical cancer.

**neuropathy**
A nerve problem that causes pain, tingling, and numbness in the hands and feet.

**observation**
A period of testing to watch for cancer growth.

**oophoropexy**
Surgery that moves one or both ovaries out of the range of the radiation beam. Also called ovarian transposition.
Words to know

**ovary**
One of a pair of organs in women that make eggs for reproduction and make hormones.

**parametrium**
The fat and connective tissue surrounding the uterus. The parametrium helps connect the uterus to other tissues in the pelvis.

**pathologist**
An expert in testing cells and tissue to find disease.

**pelvic exam**
A physical exam of the external genitalia, vagina, cervix, uterus, fallopian tubes, and ovaries.

**pelvic exenteration**
A radical surgery used to treat cervical cancer that returns to the pelvis. The uterus (including the cervix), vagina, ovaries, and fallopian tubes are removed. The bladder, rectum, and/or anus may also be removed.

**pelvis**
The area of the body between the hip bones.

**platinum agent**
A chemotherapy drug that is made with platinum. Cisplatin and carboplatin are platinum agents.

**platinum-based chemotherapy**
Treatment with two or more chemotherapy drugs and the main drug is made with platinum.

**positron emission tomography (PET) scan**
A test that uses a sugar radiotracer—a form of sugar that is put into your body and lets off a small amount of energy that is absorbed by active cells—to view the shape and function of organs and tissues inside your body.

**radiation oncologist**
A doctor who is an expert in treating cancer with radiotherapy.

**radical hysterectomy**
Surgery to remove the uterus (including the cervix) and the top quarter or third of the vagina. The connective tissue and fat surrounding the cervix is also removed.

**radiologist**
A doctor who is an expert in interpreting imaging tests.

**recurrence**
The return of cancer after treatment. Also called a relapse.

**regimen**
A treatment plan that specifies the drug(s), dose, schedule, and length of treatment.

**relapse**
The return of cancer after treatment. Also called a recurrence.

**reproductive system**
The group of organs that work together for sexual reproduction. The female reproductive system includes the ovaries, fallopian tubes, uterus, cervix, and vagina.

**squamo-columnar junction**
The area where the endocervix and ectocervix meet. Also called the transformation zone. Most cervical cancers and pre-cancers start in the squamo-columnar junction.

**squamous cell carcinoma**
Cancer that starts in squamous cells lining the ectocervix. The most common type of cervical cancer.

**supportive care**
Treatment given to relieve the symptoms of a disease. Also called palliative care.
surgical menopause
The stopping of menstrual periods caused by surgery to remove the ovaries.

targeted therapy
Treatment with drugs that target a specific or unique feature of cancer cells.

tumor
An abnormal mass formed by the overgrowth of cells.

tracelectomy
Surgery to remove the cervix. The upper part of the vagina and certain pelvic lymph nodes may also be removed.

ultrasound
A test that uses sound waves to take pictures of the inside of the body.

uterus
The organ where a fetus grows and develops during pregnancy. Also called the womb.

vagina
The hollow, muscular tube through which babies are born. Also called the birth canal.
This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cervical Cancer, Version 1.2022. It was adapted, reviewed, and published with help from the following people:

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Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

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

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

City of Hope National Medical Center
Los Angeles, 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

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

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecca.org
206.667.5000 • fredhutch.org

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

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

Mayo Clinic 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

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

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

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
901.444.5500 • uthsc.edu

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

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
858.822.8100 • 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

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

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