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FOR PATIENTS®

2023

Uterine Cancer

Endometrial Cancer

Uterine Sarcoma



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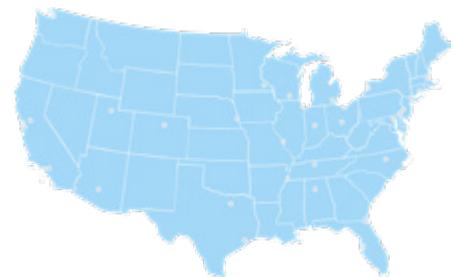


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Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The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

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms, Version 1.2023 — December 22, 2022.

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Uterine cancer basics

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There are two main types of uterine cancer. Endometrial cancer is common and can often be cured with treatment. Uterine sarcoma is rare and can be hard to treat. Both are most often diagnosed after menopause.

The most effective treatment for uterine cancer is surgery. It's important to be comfortable with your cancer care. Know that you have a choice in your treatment.

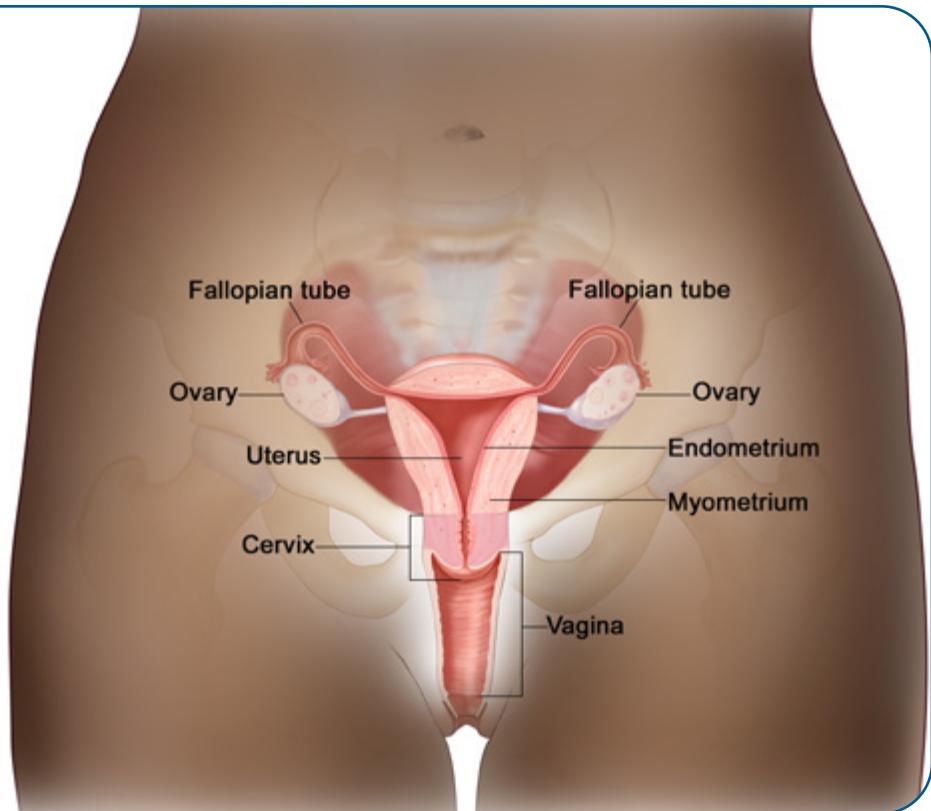
The uterus

The uterus, also sometimes called the womb, is part of the reproductive system. It is where a baby grows and develops during pregnancy. The uterus is normally about the size and shape of a pear, and is hollow in the middle. The other parts of the female reproductive system are the ovaries, the fallopian tubes, the cervix, and the vagina.

There is one ovary and one fallopian tube on each side of the uterus. The fallopian tubes connect to the top part of the uterus. The lower part of the uterus is called the cervix. The cervix connects the uterus to the vagina. Even though the cervix is part of the uterus, cancer of the cervix (cervical cancer) is diagnosed and treated differently than uterine cancer. This guide does not address cervical cancer.

The female reproductive system

The uterus, cervix, vagina, fallopian tubes, and ovaries make up the female reproductive system. The uterus is where a baby grows and develops during pregnancy.



The uterus has three main layers:

- The endometrium is the thin layer of tissue that lines the inside of the uterus.
- The myometrium is the muscular, middle layer of the uterine wall.
- The perimetrium, or serosa, is the thin, outer lining of the uterus.



Should I have been getting tested for uterine cancer?

No. Testing for a disease when you don't have any symptoms is called "screening." For example, a Pap smear is used to screen for cervical cancer and a mammogram is used to screen for breast cancer. There is currently no screening test for endometrial cancer or uterine sarcoma.

Two main types of uterine cancer

There are two main types of cancer that start in the uterus:

- Endometrial carcinoma (endometrial cancer)
- Uterine sarcoma

The differences between these types of uterine cancer are described next.

Endometrial cancer

Endometrial cancer is common and is often found before it has spread beyond the uterus. It is called endometrial cancer because it starts in the endometrium, which is the inner lining of the uterus.

The most common symptom of endometrial cancer is abnormal vaginal bleeding. Often, this means bleeding during or after menopause. Premenopausal patients may have unusually long and/or heavy menstrual bleeding (periods). For postmenopausal patients, any vaginal bleeding is abnormal and should be investigated to make sure it is not a sign of cancer.

There are different types of endometrial cancer. The most common type is called **endometrioid cancer**. Most of the information in this book and elsewhere on endometrial cancer applies to endometrioid cancer.

There are other, less common types of endometrial cancer. They grow more quickly

and are harder to treat. These high-risk endometrial cancers include:

- Serous carcinoma
- Clear cell carcinoma
- Undifferentiated/dedifferentiated carcinoma
- Carcinosarcoma, also known as malignant mixed Müllerian tumor (MMMT)

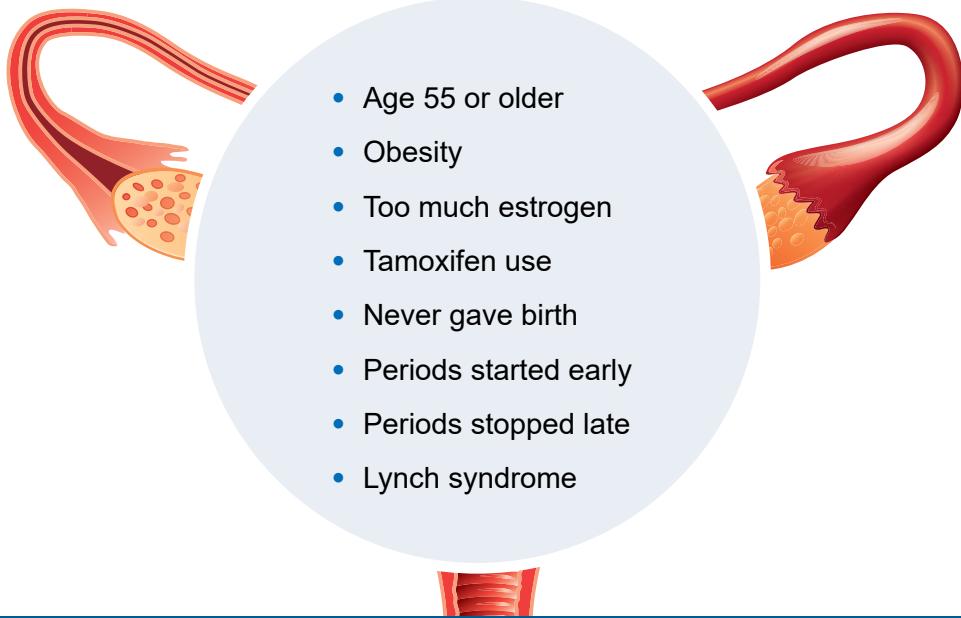
Because these cancers are more aggressive, they are treated differently than most endometrioid cancers. These types are addressed separately in ***Part 4: Endometrial cancer treatment.***

Risk factors

After being diagnosed with cancer, it is normal to wonder why it started. Some cancers are hereditary. This means that a higher risk was passed down to you by your parents through your genes. For other cancers, lifestyle plays a bigger role than genes. For many types of cancer, both genes and lifestyle play a role in whether you get that kind of cancer. The medical term for something that increases the chance of getting a disease is a risk factor. Some endometrial cancer risk factors are shown in the illustration below. Many are linked to having too much estrogen in the body.

Endometrial cancer risk factors

Many of the risk factors for endometrial cancer are related to having too much of the hormone estrogen in the body. Obesity is a major risk factor because fatty tissue in the body can change natural steroids in your body into estrogen.



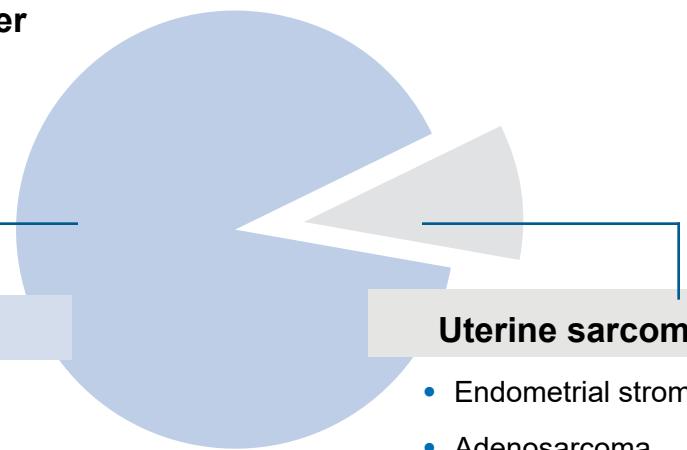
Uterine sarcoma

Uterine sarcoma starts in connective tissue cells of the uterus. It often forms in the muscle layer of the uterus (the myometrium), or in connective tissue cells in the endometrium. Uterine sarcomas are rare and may be harder to treat than endometrial cancer. They are also known as malignant mesenchymal tumors. Like endometrial cancer, there are also different types of uterine sarcomas.

This guide discusses the tumor types listed below, and others.

- Endometrial stromal sarcoma (ESS)
- Adenosarcoma
- Uterine leiomyosarcoma (uLMS)
- Undifferentiated uterine sarcoma (UUS)
- Perivascular epithelioid cell tumor (PEComa)
- Inflammatory myofibroblastic tumor (IMT)

Types of uterine cancer



Endometrial cancer

- Endometrioid carcinoma (**most common**)
- Serous carcinoma
- Clear cell carcinoma
- Carcinosarcoma, also known as malignant mixed Müllerian tumor (MMMT)
- Undifferentiated/dedifferentiated carcinoma

Uterine sarcoma

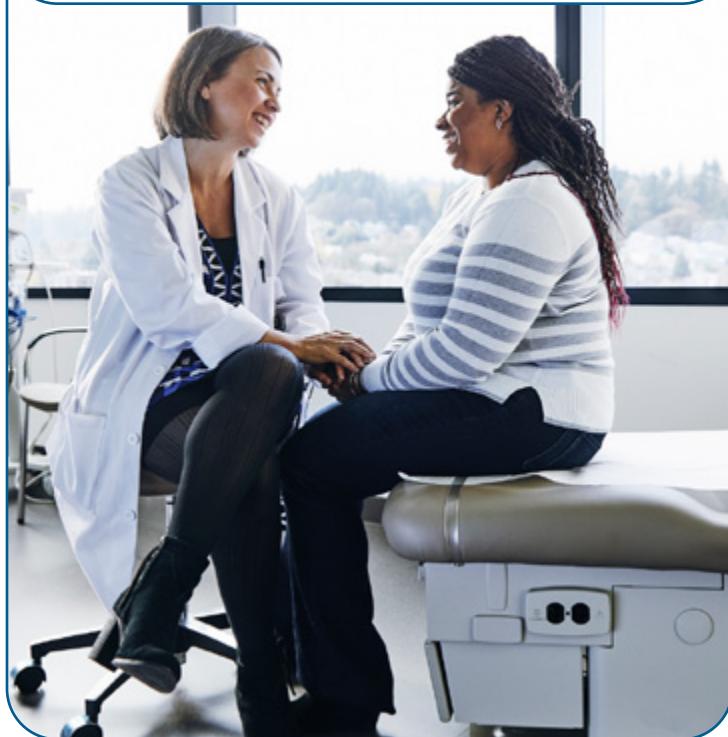
- Endometrial stromal sarcoma (ESS)
- Adenosarcoma
- Uterine leiomyosarcoma (uLMS)
- Undifferentiated uterine sarcoma (UUS)
- Perivascular epithelioid cell tumor (PEComa)
- Inflammatory myofibroblastic tumor (IMT)

Key points

The uterus

- The uterus is part of the reproductive system. A baby grows and develops in the uterus during pregnancy.
- The uterus has three main layers. From the inside out, the layers include the endometrium, the myometrium, and the perimetrium (serosa).
- There are two main types of cancer that start in the uterus: endometrial carcinoma and uterine sarcoma.

Create a personal relationship with your care team. Believe in their skills and dedication to help you! They are your greatest asset.



Endometrial cancer

- Endometrial cancer is common and is often found early. The most common symptom is abnormal vaginal bleeding.
- Endometrioid is the most common type of endometrial tumor.
- High-risk endometrial cancers include serous carcinoma, clear cell carcinoma, undifferentiated/dedifferentiated carcinoma, and carcinosarcoma.
- These less common types grow more quickly and are harder to treat.

Uterine sarcoma

- Uterine sarcoma starts in the wall or muscles of the uterus.
- This type of uterine cancer is rarer and more aggressive than endometrial cancer.
- Uterine sarcomas are often found after a hysterectomy.

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Testing for uterine cancer

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- 14 Tumor tissue tests
- 15 Key points

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 the tests you may need and other steps needed to create your treatment plan.

If uterine cancer is suspected or confirmed, your doctor will do a complete physical exam. This often includes a pelvic exam to check the size and mobility of your uterus. Your doctor will want to know a lot about on your past and current health. They will also ask you about symptoms that could be related to uterine cancer, such as vaginal bleeding.

Biopsy

Endometrial biopsy

If you have vaginal bleeding or other possible symptoms of uterine cancer, an endometrial biopsy is typically performed. This can usually be done in your gynecologist's office. Endometrial biopsy involves removing a sample of tissue from the lining of the uterus (the endometrium). The removed tissue is examined by a specialized doctor called a pathologist. The pathologist determines the cancer type and subtype, when possible. Endometrial biopsy is much better at diagnosing endometrial cancer than it is at diagnosing uterine sarcoma.

Cervical biopsy

If your doctor thinks that the cancer may have spread to the cervix, you will likely have a cervical biopsy. This is similar to an endometrial biopsy, but the cells are taken from the cervix instead of from the endometrium.

Blood tests

A complete blood count (CBC) is a common blood test. It provides information about the numbers 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. Your blood counts may be high or low because of cancer or other problems.

You may also have a blood test called a chemistry profile. It measures the amount of certain substances in the blood, such as metabolites, electrolytes, fats, and proteins. This test provides information about how well your kidneys, liver, and other organs are working.

Imaging

Ultrasound

Ultrasound uses sound waves to make pictures of the inside of the body. It is good at showing the size, shape, and location of the uterus.

There are two types of ultrasounds that may be used to evaluate uterine cancer. In a transabdominal ultrasound, a gel will be spread onto your stomach and the area between your hip bones. The gel helps to make the pictures clearer. Your doctor or technician will place the probe on your skin and guide it back and forth in the gel.

For a transvaginal ultrasound, the probe will be inserted into your vagina. This may help your doctor see the uterus and nearby areas more clearly. Ultrasounds are generally painless. You may feel some discomfort when the probe is inserted.

A CT scan is a more detailed type of x-ray. It is painless and noninvasive. CT makes many images from different angles. A computer combines the images to make 3-D pictures.

Chest x-ray

If endometrial cancer is suspected or confirmed, you may have a chest x-ray. The purpose is to look for signs of disease in and around the chest. X-rays are painless and use a very small amount of radiation. If any abnormal or suspicious areas are found, a computed tomography (CT) scan of your chest may be ordered to get a better look. CT is described next.

CT

You may have a CT scan of your chest, abdomen, and pelvis. Your doctor is looking for signs of cancer spread in these areas, especially for higher-risk tumors.

A CT scan is a more detailed kind of x-ray. It takes many pictures from different angles. A computer combines the images to make three-dimensional (3-D) pictures.



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. You may also be asked to drink a liquid contrast to highlight the bowel. 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 scan

If your doctor suspects that the cancer has spread beyond the pelvis (metastasized), CT 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.

Pelvic MRI

You may have magnetic resonance imaging (MRI) of your pelvis. An MRI can show the tissues of the uterus and cervix closely. An MRI may show whether the cancer has spread to the cervix or other nearby organs. 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 chest x-ray, MRI does not use radiation. Tell your doctor if you get nervous in tight spaces.

MRI makes pictures of areas inside the body without using radiation. An MRI can show the tissues of the uterus and cervix closely. Tell your care team if you get nervous in enclosed spaces.



Family history and genetic testing

Most endometrial cancers are caused by random (non-hereditary) mutations in DNA. Only about 5 out of 100 are due to an inherited risk. However, your doctor will want to know if you have a family history of cancer, or of other diseases that can raise your risk of getting cancer. Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), is an inherited cancer syndrome.

Lynch syndrome is strongly linked to colorectal, endometrial, ovarian, and other cancers. Endometrial cancer tends to start about 10 to 20 years earlier in those with Lynch syndrome compared to those without an inherited risk. Li-Fraumeni syndrome (LFS) is another hereditary cancer risk syndrome. People with LFS are at higher risk of developing uterine sarcoma. To determine who should be tested for Lynch syndrome, the tumor is tested for mismatch repair (MMR) protein expression.

Mismatch repair (MMR)

In normal cells, a process called MMR fixes errors that happen when the DNA divides and makes a copy of itself. If a cell's MMR system isn't working right, errors build up and cause the DNA to become unstable. This is called microsatellite instability (MSI).

There are two kinds of lab tests for this biomarker. Depending on the method used, an abnormal result is called either microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR). Tumors that are not dMMR/MSI-H are referred to as microsatellite stable (MSS) or mismatch repair proficient (pMMR).

MMR/MSI testing is recommended for everyone diagnosed with endometrial

cancer, and may be ordered for uterine sarcomas. Testing is performed on either the biopsy sample or on the tumor removed during surgery. If the cancer is dMMR/MSI-H, you may also be tested for Lynch syndrome.

If the tumor does not have abnormal MMR results but you have a strong family history of endometrial and/or colorectal cancer, genetic counseling and testing for inherited (germline) mutations is recommended. If you have Lynch syndrome or LFS, you will be monitored closely and counseled on ways to reduce the risk of getting other cancers.

Tumor tissue tests

Hormone receptor testing

Some cancer cells have proteins to which the hormones estrogen and progesterone can attach. These proteins are called receptors. Once attached, the hormones may help the cancer grow or inhibit growth. Knowing whether the tumor cells have hormone receptors may affect treatment planning.

Testing involves analyzing a small piece of the tumor in a lab. If the tumor cells have hormone receptors, the cancer is called estrogen and/or progesterone receptor “positive.” Hormone receptor testing is recommended for most uterine sarcomas, and for recurrent or advanced endometrial cancer.

HER2

HER2 is a protein found on the surface of cells. Some endometrial cancers have too much of a protein called HER2. This causes the cancer to grow and spread quickly. HER2 testing is recommended for certain advanced or recurrent high-risk endometrial tumors.

Key points

Biopsy

- Endometrial cancer is typically diagnosed using endometrial biopsy. This involves removing a sample of tissue from the lining of the uterus (the endometrium).
- Endometrial biopsy is generally good at diagnosing endometrial cancer, but is not as reliable for diagnosing uterine sarcoma.

Other testing

- Other testing before treatment includes a physical exam, health history, and blood tests.
- Imaging tests may also be recommended and could include ultrasound, chest x-ray, CT, pelvic MRI, and possibly PET/CT.

Family history and genetic testing

- Most endometrial cancers are caused by random (non-hereditary) mutations in DNA.
- Lynch syndrome is an inherited syndrome strongly linked to colorectal, endometrial, ovarian, and other cancers.
- Tell your doctor if you have a family history of cancer, or of other diseases that can raise your risk of getting cancer.
- To determine who should be tested for Lynch syndrome, the tumor is tested for MMR protein expression.
- MMR/MSI testing is recommended for everyone diagnosed with endometrial cancer.

Tumor tissue tests

- Hormone receptor testing is recommended for most uterine sarcomas and for advanced (stage III or IV) or recurrent endometrial cancer.
- Hormone receptor testing is performed after surgery using the tumor that was removed.

3

Treatments for uterine cancer

- 17 Surgery
- 18 Surgical staging
- 24 Radiation therapy
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- 27 Clinical trials
- 29 Key points

In this chapter, the main treatments for uterine cancer are described. Your treatment options will depend on whether you are a candidate for surgery and other factors.

Surgery

When possible, surgery is the preferred treatment for uterine cancer. The most common surgery is total hysterectomy and bilateral salpingo-oophorectomy (BSO). A total hysterectomy removes the uterus, including the cervix. A BSO removes both ovaries and both fallopian tubes.

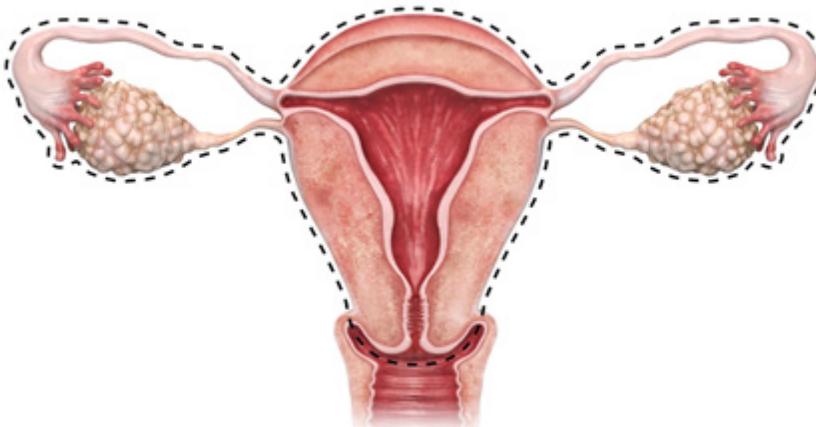
Carrying a pregnancy is not possible after a hysterectomy. Fertility-sparing therapy may be an option if you desire it. More information on fertility-sparing treatment is provided in **Part 4: Endometrial cancer treatment**.

Less commonly used surgeries for uterine cancer include:

- **Radical hysterectomy:** The uterus, the cervix, some of the tissues next to the cervix, and part of the vagina are removed.
- **Total hysterectomy and unilateral salpingo-oophorectomy (USO):** The uterus, cervix, and one ovary and one fallopian tube are removed.
- **Total hysterectomy and bilateral salpingectomy (BS):** The uterus, cervix, and both fallopian tubes are removed. The ovaries are left in the body.

Total hysterectomy and BSO

The most commonly used surgery for uterine cancer removes the uterus (including the cervix), both ovaries, and both fallopian tubes.



Minimally invasive surgery involves making only a few small cuts into your body to do the surgery. With minimally invasive surgery there is usually less pain and scarring. Also, the time it takes to recover is usually shorter compared to surgery that uses a larger cut through the abdomen. Minimally invasive surgery may be an option depending on the type and extent of the uterine cancer.

Sometimes the tumor ends up being larger than expected or spreads to other locations. In this case, tumor debulking may be an appropriate treatment.

In tumor debulking surgery, the surgeon attempts to remove all cancer that can be seen or felt. Tumor debulking surgery is considered successful if all tumor is removed, or if all tumor is removed except implants measuring up to 1 cm (optimal debulking).

When it is safe, debulking is a good idea for endometrial cancer because it may mean that other treatments have a better chance of killing the leftover tumor cells.

Surgical staging

During surgery, your surgeon will look very closely at the tissues and organs closest to the pelvis for signs of cancer and take samples of any suspicious areas for testing.

Your surgeon may put fluid in the open space of your abdomen and then remove it to see if it has cancer cells. This is called peritoneal washing. Lymph nodes are often removed and tested for cancer. This may be done using a procedure called a sentinel lymph node biopsy.

The information gained first-hand during surgery is used, along with tests done before surgery, to determine the stage (extent) of the

cancer. This process is called surgical staging. The cancer stage helps your doctors decide if you need further treatment after surgery.

There are two systems used to stage uterine cancer—the International Federation of Gynecology and Obstetrics (FIGO) system and the American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) system. Both systems use the following key pieces of information about your cancer in order to give it a stage:

- The size or extent/depth of the tumor
- Whether any lymph nodes have cancer
- Whether the cancer has spread to other parts of your body (metastasized)

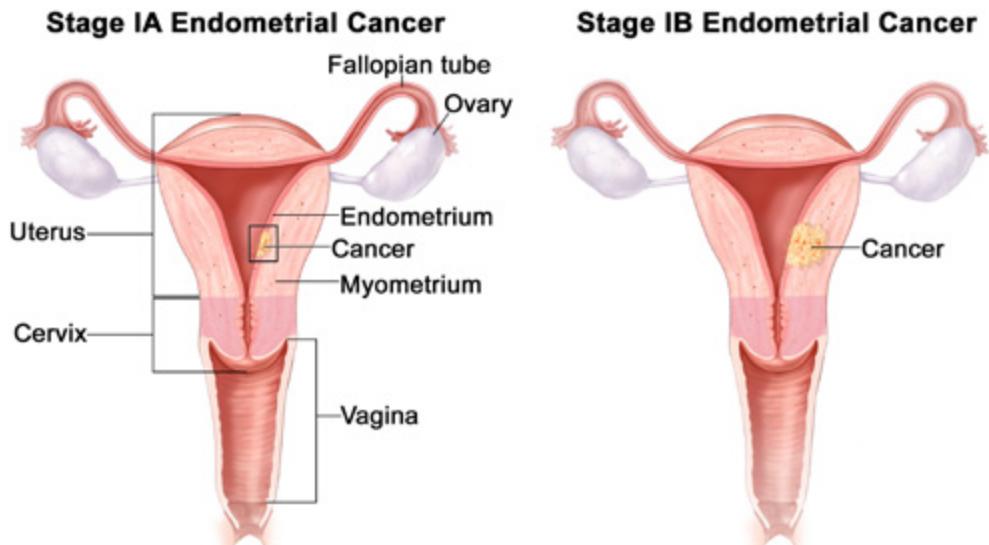
There are four main stages of endometrial cancer and uterine sarcoma. The stages of each are described in more detail next. In general, people with earlier cancer stages have better outcomes, but not always. Some people will do better than expected for their stage, and some people will do worse.

Endometrial cancer stages

There are four main stages of endometrial cancer in the FIGO staging system: I, II, III, and IV. Some of the stages are broken down into sub-stages that have letters and may also have a number. Examples are stage IIIB and stage IIIC2. The stages are shown in the illustrations on the following pages.

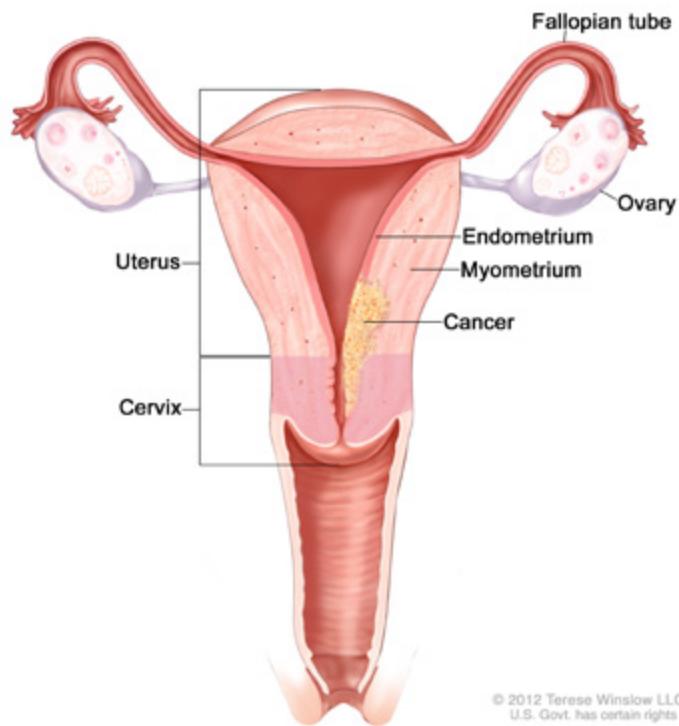
Stage I endometrial cancer

The tumor is in the main body of the uterus. It has not grown into the cervix.



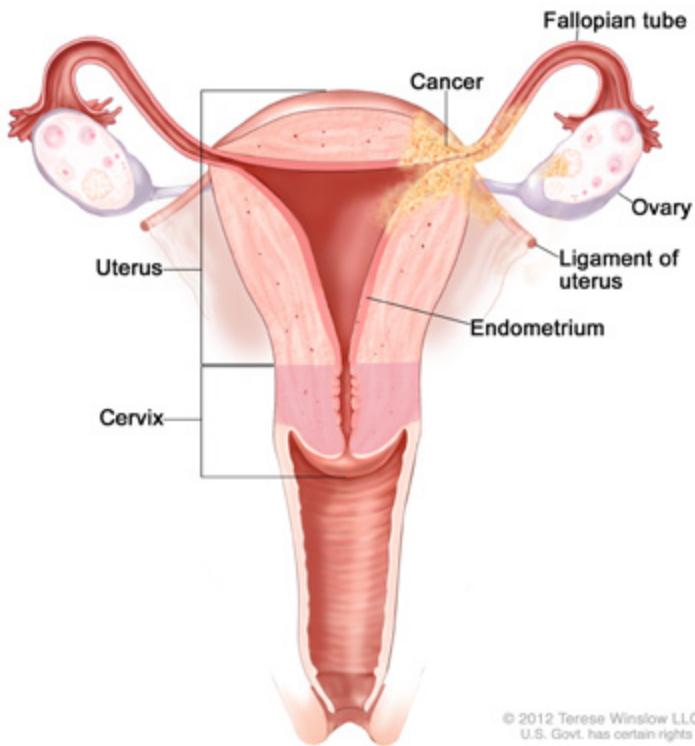
Stage II endometrial cancer

The tumor has grown into the cervix.



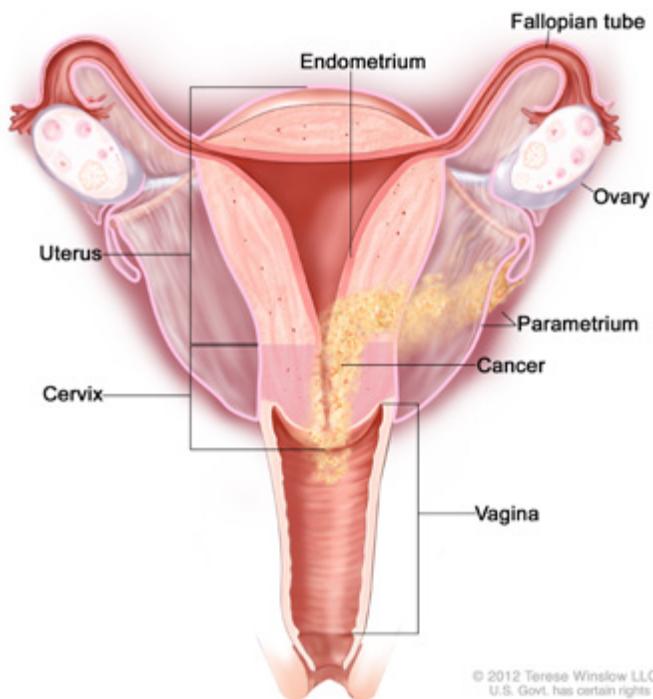
Stage IIIA endometrial cancer

The tumor has grown into the outer layer of the uterus, the ovaries, or the fallopian tubes.



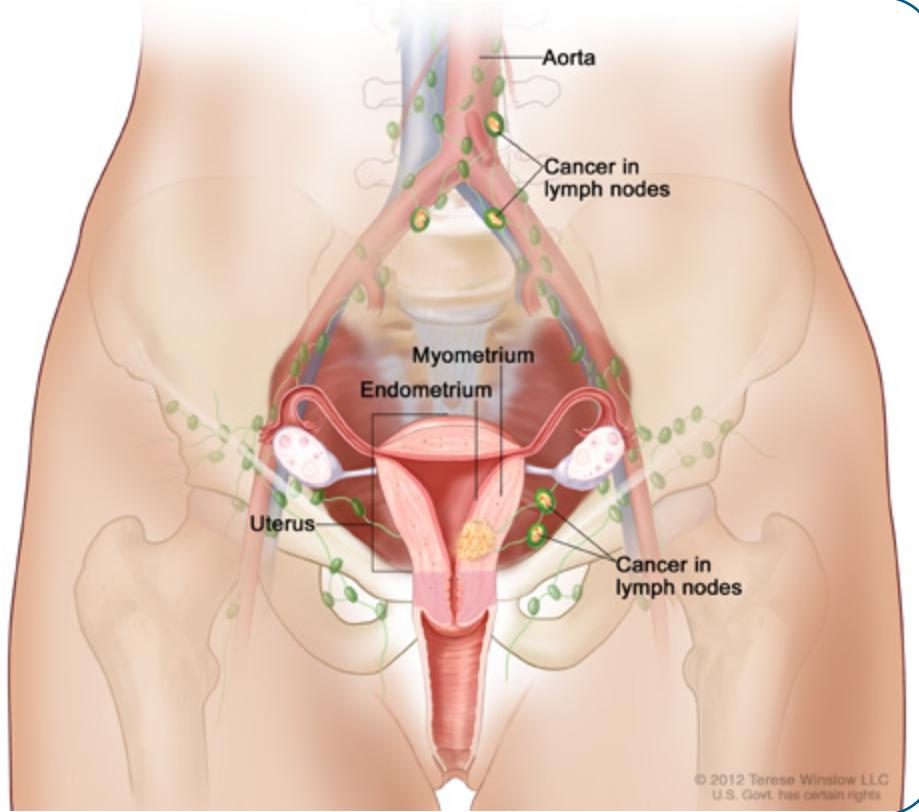
Stage IIIB endometrial cancer

There is cancer in the vagina, or in the fat and connective tissue around the uterus.



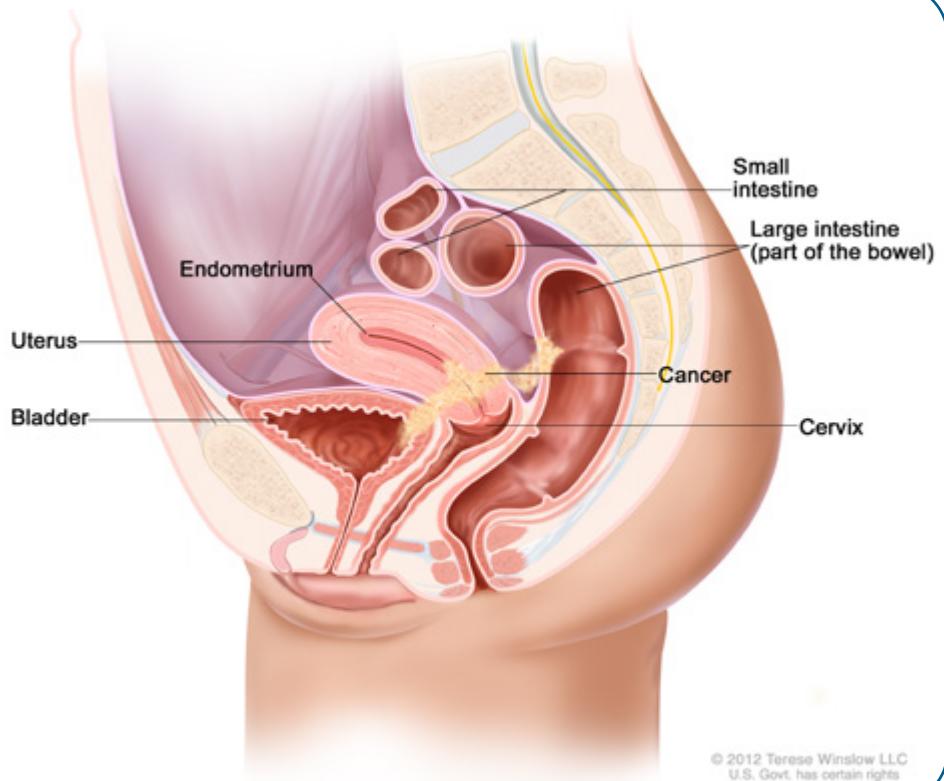
Stage IIIC endometrial cancer

There is cancer in the lymph nodes closest to the uterus, called the **pelvic lymph nodes** (stage IIIC1) or in the lymph nodes near the bottom of the spine, called the **para-aortic lymph nodes** (stage IIIC2).



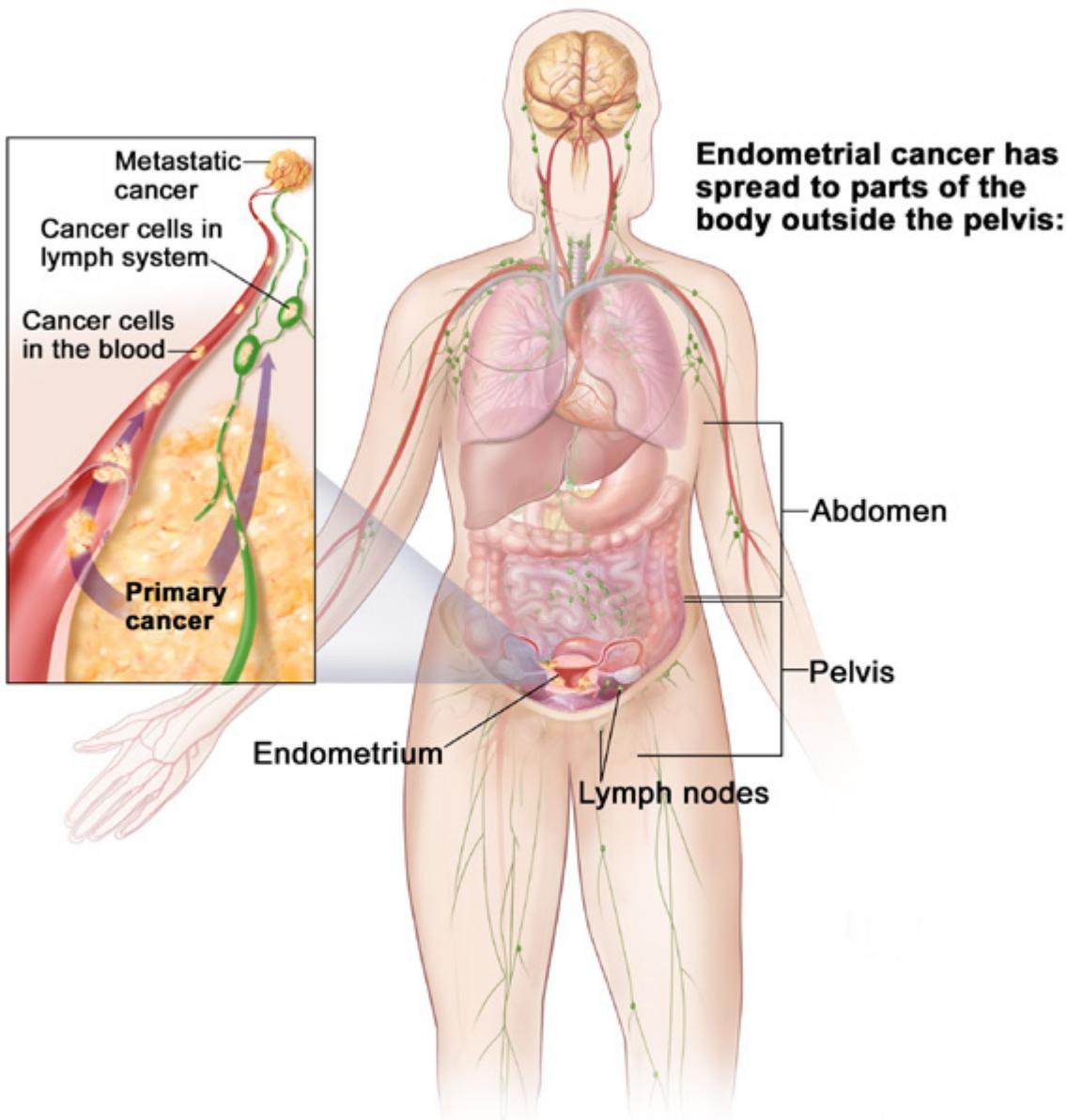
Stage IVA endometrial cancer

Cancer has spread to the lining of the bladder or intestines.



Stage IVB endometrial cancer

Cancer has spread to areas far from the uterus, such as the abdomen, the bones, or the lungs. The abdomen includes the pancreas, stomach, intestines, liver, and gallbladder.



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Uterine sarcoma stages

There are four main stages of uterine sarcoma in the FIGO staging system: I, II, III, and IV.

All of the stages are broken down into lettered sub-stages. **See Guide 1.**

Guide 1

Stages of leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and adenosarcoma

Stage I - The tumor is small and only in the uterus.

IA	For LMS and ESS: The tumor is 5 centimeters (about 2 inches) or smaller. For adenosarcoma: The tumor is only in the endometrium.
IB	For LMS and ESS: The tumor is bigger than 5 centimeters. For adenosarcoma: The tumor has grown less than halfway through the myometrium.
IC	Adenosarcoma: The tumor has grown more than halfway through the myometrium.

Stage II - The tumor has spread beyond the uterus, but is still in the pelvis.

IIA	The tumor has grown into the ovaries or the fallopian tubes.
IIB	The tumor has also grown into other tissues in the pelvis.

Stage III - There is cancer in the abdomen and possibly in nearby lymph nodes.

IIIA	The tumor has grown into one area of the abdomen.
IIIB	The tumor has grown into two areas of the abdomen.
IIIC	There is cancer in nearby lymph nodes.

Stage IV - There is cancer in the bladder or rectum and possibly in areas far from the uterus.

IVA	The tumor has grown into the bladder or rectum.
IVB	Cancer has spread to areas far from the uterus, such as the lungs.

Radiation therapy

Radiation therapy uses high-energy waves similar to x-rays to kill cancer cells. It is a commonly used treatment for both endometrial cancer and uterine sarcoma. The types of radiation therapy that may be used to treat uterine cancer are described next. You may have treatment with more than one type.

External beam radiation therapy

In external beam radiation therapy (EBRT), a large machine aims radiation at the cancer site. The radiation passes through skin and other tissue to reach the tumor. EBRT is given in small doses, called fractions. For the treatment of uterine cancer, EBRT is typically given 5 days a week for 5 to 6 weeks.

A planning session, called simulation, is needed before treatment begins. You will first be 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 sites will be obtained with a CT scan. Using the CT scan pictures and sophisticated computer software, your radiation oncologist will make a treatment plan to aim radiation beams at the tumor and nearby lymph nodes. The plan will describe the best radiation dose for you, as well as the number of sessions you will need.

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 on your skin will help position your body accurately for daily treatments. You will be alone in the treatment room. A technician will operate the machine from a nearby room. The technician will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. You will not see, hear, or feel the radiation. One session takes about 20 minutes and the beam is on for about two minutes.

External beam radiation therapy (EBRT)

A large machine aims radiation at the tumor, passing through skin and other tissue to reach it.



IMRT

An advanced type of EBRT called intensity-modulated radiation therapy (IMRT) may be used to treat uterine cancer. IMRT uses many small beams of different 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 and bladder. This can help reduce treatment-related side effects.

SBRT

Stereotactic body radiotherapy (SBRT) is a highly specialized type of EBRT. It may be used to treat endometrial cancer that has spread to the liver, lungs, or bone. High doses of radiation are delivered to a metastatic site or sites using very precise beams. SBRT is typically delivered in 5 or fewer sessions.

Stereotactic radiosurgery (SRS)

SRS is a non-surgical and highly precise type of radiation therapy. It can be used to treat small brain or spine tumors.

Side effects

Common side effects at the treatment site during the 5 to 6 weeks of external radiation treatment include skin irritation, tenderness, and redness. Other short-term side effects of radiation therapy include fatigue, diarrhea, frequent urination or pain while urinating, and nausea. Most of these decrease over time when treatment is over. Radiation therapy side effects may not be felt right away. They may appear and worsen later in the cycle or even after it is complete.

Radiation therapy for uterine cancer can also have long-term and possibly serious side effects on fertility, sexual health, and bowel and bladder function. See **Part 6:**

Survivorship for information on ways to help prevent, limit, or manage these effects.

Brachytherapy

Another type of radiation therapy used for uterine cancer is called brachytherapy, or internal radiation. It is called internal because the cancer-fighting radioactive material is put inside your body, either directly into the tumor or close to it. Hollow tubes are placed in the vagina or uterus and a small radiation pellet travels to the region of the tumor. This may be done several times to deliver a safe dose.

Systemic therapy

Systemic therapy is treatment with substances that travel in the bloodstream, reaching and affecting cells throughout the body. Types of systemic therapy include chemotherapy, targeted therapy, immunotherapy, and endocrine therapy.

Chemotherapy, targeted therapy, and immunotherapy

Chemotherapy is the most commonly used type of systemic therapy for uterine cancer. It stops the growth of cancer cells, either by killing the cells or by stopping them from dividing. Most chemotherapy drugs are given by infusion. This means they are liquids slowly injected into the bloodstream through a vein.

Targeted therapy and immunotherapy are newer types of systemic therapy. They may be treatment options for uterine cancer that does not respond to chemotherapy, returns after treatment with chemotherapy (recurrent), or spreads beyond the pelvis (metastatic). Unlike chemotherapy, targeted therapy and immunotherapy are most effective at treating cancers with specific features, called biomarkers.

Chemotherapy, targeted therapy, and immunotherapy can kill healthy cells in addition to cancer cells. The damage to healthy cells causes potentially harsh side effects, such as hair loss, cracked skin, and mouth sores.

These types of systemic therapy are often given in cycles of treatment days followed by days of rest. This allows your body to recover before the next cycle. For example, you might receive chemotherapy every day for 1 week followed by 3 weeks with no chemotherapy. These 4 weeks make up one cycle. Cycles vary in length depending on which drugs are used.

Endocrine therapy

Estrogen and progesterone are hormones. They can affect the growth of cancer cells in the uterus. Endocrine therapy is a type of cancer treatment that changes the levels of certain hormones in the body. It's not the same as the hormone therapy that may be used to manage symptoms of menopause, called hormone replacement therapy (HRT).

The types of endocrine therapy that may be used for uterine cancer are described next.

Progestins are lab-made versions of the hormone progesterone. They help slow the growth of endometrial cancer cells. Progestins used to treat some uterine cancers include:

- Medroxyprogesterone acetate (Provera) – taken orally
- Megestrol acetate – taken orally
- Levonorgestrel (Mirena), a progestin-releasing intrauterine device (IUD)

Aromatase inhibitors are oral medications. They can stop estrogen from being made by fatty tissue in the body. As a result, the overall amount of estrogen in the body is lowered. Aromatase inhibitors include:

- Anastrozole (Arimidex)
- Letrozole (Femara)
- Exemestane (Aromasin)

Tamoxifen is a drug used to reduce the amount of estrogen in the body. It is taken orally. Tamoxifen is not used for uterine sarcoma.

Fulvestrant (Faslodex) blocks estrogen receptors that can cause cancer cells to grow. Fulvestrant is given by injection (shot).

Gonadotropin-releasing hormone (GnRH) agonists work by lowering estrogen levels in those with functioning ovaries.

Side effects

Endocrine therapy can cause side effects. Symptoms of menopause are common. Such symptoms include hot flashes, changes in mood, vaginal dryness, trouble sleeping, and night sweats. Other common side effects of endocrine therapy are vaginal discharge, weight gain, swelling in the hands and feet, fatigue, and reduced interest in sex. Blood clots are a rare but serious side effect of tamoxifen. Aromatase inhibitors can weaken your bones and may also cause joint and muscle pain.

Ask your treatment team for a full list of common and rare side effects of each systemic therapy you are receiving.

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.

Do I have to pay to be in a clinical trial?

Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.



Finding a clinical trial

In the United States

GOG Foundation

gog.org

NCCN Cancer Centers

NCCN.org/cancercenters

The National Cancer Institute (NCI)

cancer.gov/about-cancer/treatment/clinical-trials/search

NRG Oncology

nrgoncology.org

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

Key points

Surgery and staging

- Total hysterectomy with bilateral salpingo-oophorectomy (BSO) is the most commonly used surgery for uterine cancer.
- The results of surgery and testing are used to stage the cancer. This is called surgical staging.
- The stage describes how much cancer there is in the body and where it has spread.
- Endometrial cancer and uterine sarcoma are staged differently. Each type has four main stages.

Radiation therapy

- Radiation therapy uses high-energy rays to kill cancer cells or stop new cancer cells from being made.
- External beam radiation therapy (EBRT) and vaginal brachytherapy are commonly used to treat uterine cancer.

Systemic therapy

- Systemic therapy is treatment with substances that travel through the bloodstream, reaching and affecting cells all over the body.
- Chemotherapy, endocrine therapy, targeted therapy, and immunotherapy are types of systemic therapy.

Clinical trials

- Clinical trials give people access to investigational tests and treatments that may, in time, be approved by the FDA.

4

Endometrial cancer treatment

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- 41 Recurrence
- 44 Key points

This chapter presents the recommended treatment options for endometrial cancer. Treatment for the most common type of endometrial tumor (endometrioid) is discussed first, followed by treatment for high-risk types.

Before starting treatment, it is important to know if the cancer has spread. If it has (and how far) plays a role in how it is treated. There are three main possibilities:

- The cancer is only in the main part of the uterus (not the cervix).
- The cancer has grown into the cervix.
- The cancer has spread beyond the uterus into other parts of your body.

Treatment for each of these scenarios is discussed next.

Endometrioid cancer

Cancer is only in the uterus

Endometrial cancer is often found before it has spread beyond the body of the uterus. In this case, the most effective treatment is surgery. If you are willing and able to have surgery, a total hysterectomy (TH) with bilateral salpingo-oophorectomy (BSO) is recommended. TH removes the uterus and cervix. It is necessary to remove the cervix because uterine cancer can extend into the cervix. BSO removes both ovaries and fallopian tubes. It may be possible to keep your ovaries. Ovary preservation is discussed more below.

Carrying a pregnancy is not possible after a hysterectomy. If pregnancy is possible and desired, fertility-sparing treatment may be an option. See the next page for more information.

When possible, minimally invasive surgery is preferred for endometrioid cancer that has not spread beyond the body of the uterus. During surgery, your surgeon will assess the extent of the cancer and remove tissue and lymph nodes for testing. The results of surgery and testing are used to stage the cancer. This is called surgical staging. The stage is used to determine treatment needed after surgery. See **Treatment after surgery** on page 36 for next steps.

Ovary preservation

Prior to menopause, the ovaries produce the hormones estrogen and progesterone. Removing the ovaries causes a sudden loss of estrogen. This is known as surgical menopause. Side effects of surgical menopause include hot flashes, sleeping problems, changes in mood, and vaginal atrophy. Vaginal atrophy is a condition in which

the lining of the vagina becomes thin, dry, and inflamed.

There are also long-term risks of not having enough estrogen. These include heart or blood vessel problems (cardiovascular disease) and bone loss (osteoporosis).

If you are premenopausal, it may be safe for you to keep your ovaries. This is called ovarian preservation. This may be an option if:

- The cancer is stage I
- Your ovaries look normal on imaging tests
- You do not have a family history of breast cancer, ovarian cancer, or Lynch syndrome

If you are able to keep your ovaries, it is still recommended that the fallopian tubes be removed with the uterus.

You decline or cannot have surgery first

If you do not want surgery or are unable to have it for other health reasons, treatment with radiation therapy is preferred. External beam radiation therapy (EBRT), brachytherapy (internal radiation), or both may be used.

Another option is endocrine (hormone) therapy. Hormone therapy is typically only considered for small or slow-growing endometrioid tumors. Oral progestins such as medroxyprogesterone acetate (Provera) and megestrol acetate are preferred. In some cases, a progestin-releasing intrauterine device (IUD) may be a better option. Mirena is an example. It contains the progestin levonorgestrel.

Fertility-sparing therapy

Surgery to remove the uterus, cervix, fallopian tubes, and ovaries is the standard treatment for endometrial cancer that has not spread beyond the uterus. Carrying a pregnancy is not possible without a uterus. For some people

diagnosed with endometrial cancer, this can be hard to accept.

If you have low-risk endometrial cancer and want to treat the cancer, but also want to try to have a child in the future, fertility-sparing treatment may be an option. It involves delaying surgery and treating the cancer with hormone therapy first. If hormone therapy works well and kills all of the cancer, you can try to become pregnant.

Fertility-sparing therapy is only an option for some low-risk endometrial cancers. It may be an option if:

- The tumor is endometrioid (the most common type).
- Imaging tests show that the cancer does not extend beyond the endometrium.
- The cancer cells are grade 1. This means that they look similar to healthy cells under a microscope.
- There are no medical reasons why you cannot (or should not) get pregnant.
- There are no medical reasons why you cannot or should not have hormone therapy. Contraindications to hormone therapy include stroke, myocardial infarction, pulmonary embolism, deep vein thrombosis, and smoking.
- You fully understand that fertility-sparing therapy is not the standard treatment for endometrial cancer.
- You agree to regular endometrial biopsies to check if the treatment is working.

Before starting fertility-sparing therapy, consulting with a fertility expert is recommended. You may also have genetic counseling and testing.

It is important to maintain a healthy weight and lifestyle during fertility-sparing therapy. It may lead to better treatment outcomes. Expect your doctor to ask about your diet, level of activity, and other lifestyle-related factors.

There are 3 options for hormone therapy. All use artificial versions of the hormone progesterone:

- Medroxyprogesterone acetate (Provera) – taken orally
- Megestrol acetate – taken orally
- Progestin intrauterine device (IUD), such as Mirena

To see if hormone therapy is working, a tissue sample will be removed from the endometrium every 3 to 6 months for testing. This is done using endometrial biopsy or dilation and curettage (a “D&C”).

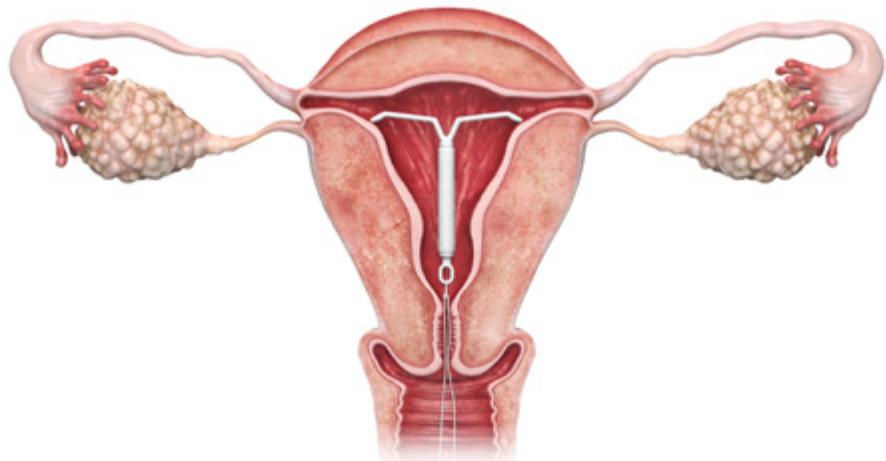
If hormone therapy works well and the cancer is gone after 6 months, you can stop hormone therapy and begin trying to get pregnant. While you are trying to get pregnant, you will continue to have testing of your endometrium every 6 months.

If hormone therapy was successful but you do not start trying to conceive right away, your doctor may recommend continuing progestin-based hormone therapy in order to maintain the good results. If the cancer returns while you are trying to get pregnant, your doctor will recommend that you have the surgery.

If the hormone therapy does not work and the cancer is still there after 6 to 12 months, surgery is recommended. Keeping your ovaries may be an option.

Intrauterine device (IUD)

An IUD that releases levonorgestrel is one method of hormone therapy used in fertility-sparing therapy.



Cancer has spread to the cervix

If a cervical biopsy or pelvic magnetic resonance imaging (MRI) shows that the cancer has grown into the cervix, treatment options depend on whether surgery can be performed first. When possible, having surgery first is preferred.

If you agree to surgery and are healthy enough to have it, either a total hysterectomy or a radical hysterectomy is recommended, along with BSO to remove the fallopian tubes and ovaries.

Your surgeon will assess the extent of the cancer during surgery and remove tissue and lymph nodes for testing. Pathologists will examine the removed tissue and determine the cancer stage. This is known as surgical staging. The stage is used to determine treatment needed after surgery. See **Treatment after surgery** on page 36 for next steps.

In some cases, both EBRT and brachytherapy may be used first to try to shrink the cancer before surgery. However, going straight to surgery is usually advised when possible. If radiation therapy is given before surgery, it will not be given again after surgery. See **When treatment is over** on page 40 for next steps.

You decline or cannot have surgery first

If you do not want to have surgery or are unable to have it for other health reasons, there are other treatment options. Most commonly, radiation therapy is used first to try to shrink the tumor. Both EBRT and brachytherapy are given. Platinum-based chemotherapy may be given in addition to radiation therapy. When given with radiation, chemotherapy can make it easier for radiation to kill cancer cells. The combined use of these treatments is called chemoradiation. If

treatment with radiation (and chemotherapy, if given) works well, surgery may be an option if you agree to have it.

Another option for those who cannot have surgery first is chemotherapy alone to try to shrink the cancer. The regimen preferred at this time is carboplatin and paclitaxel together. If it works well, surgery may be an option. If surgery is still not possible, treatment with both EBRT and brachytherapy is recommended.

Cancer has spread beyond the uterus

Treating cancer that has spread beyond the uterus depends on how far the cancer has spread and whether it can be removed with surgery first.

You are willing and able to have surgery first

If the cancer has not spread beyond the pelvis or abdomen, total hysterectomy and BSO are recommended. Your surgeon will try to remove as much of the cancer as possible. Some people have chemotherapy before surgery to try to shrink the tumor.

During surgery, your surgeon will assess the extent of the cancer and remove tissue and lymph nodes for testing. Pathologists will examine the removed tissue and determine the cancer stage. This is known as surgical staging. The stage is used to determine treatment needed after surgery. Endometrial cancer that has spread beyond the uterus is either stage III or IV. See **Treatment after surgery** on page 36.

If the cancer has spread to areas far from the pelvis (metastasized), systemic therapy is recommended. At this time, the preferred regimen is carboplatin and paclitaxel together. EBRT may be used in addition to

chemotherapy. Surgery (total hysterectomy and BSO) may also be considered, but not with the goal of curing the cancer. The purpose is to relieve symptoms caused by the cancer and further limit its spread. This is called palliative surgery. If surgery is planned, stereotactic body radiation therapy (SBRT) may be used to destroy small metastatic tumors. See ***When treatment is over*** on page 40 for next steps.

You decline or cannot have surgery first

If you do not want surgery or cannot have it for other health reasons, treatment options depend on how far the cancer has spread. If the cancer has not spread beyond the pelvis or abdomen, EBRT may be recommended. Brachytherapy, systemic therapy, or both may be given in addition to external radiation. If treatment works well, surgery may be possible if you are willing to have it.

If the cancer has metastasized, systemic therapy is recommended. If it works well, surgery may be possible if you are willing to have it. Otherwise, treatment with radiation therapy may be an option.



Is endometrial cancer hereditary?

Not usually. Most cases of endometrial cancer are caused by random (non-hereditary) mutations in DNA. Only about 5 out of 100 endometrial cancers are due to an inherited risk. This includes people with an inherited disorder called Lynch syndrome. People with Lynch syndrome have a high risk (about 60%) of getting endometrial cancer in their lifetime. Patients with Lynch syndrome should be monitored closely and counseled on ways to reduce the risk of getting endometrial and other cancers.

Treatment after surgery

The treatment(s) you may have after surgery are described next, according to the stage. This information applies to endometrioid cancers only.

Stage I

Treatment is recommended after surgery for some stage I endometrioid cancers. Your doctor will consider the factors listed below to determine if more treatment may help lower the risk of the cancer returning.

- The cancer stage (IA or IB)
- The cancer grade (how abnormal the tumor cells look under a microscope)
- Your age
- How far the tumor extends into the muscle layer of the uterus (if at all)
- Whether there are tumor cells in the blood vessels or lymph vessels outside of the main tumor, known as lymphovascular space invasion (LVSI). If there are, it means that the cancer is more likely to have spread to the lymph nodes.

After weighing these factors, your doctor may decide that you don't need more treatment. In this case, a watch-and-wait approach is used. Surveillance will begin.

If you do need more treatment, the main treatments used after surgery for stage I endometrial cancer are:

- Vaginal brachytherapy
- EBRT

For some high-grade, stage IB endometrioid tumors, chemotherapy may be given in addition to one or both of the above

treatments. After any treatment given after surgery, follow-up care begins.

Stage II

Radiation therapy is recommended after surgery for all stage II endometrial cancers. EBRT is preferred. Vaginal brachytherapy is also an option and may be given alone or in addition to EBRT. Vaginal brachytherapy alone may be considered for very low-risk stage II cancers. In some cases, either chemotherapy or hormone therapy is given in addition to EBRT and/or vaginal brachytherapy. Hormone therapy is typically only considered for small or slow-growing endometrioid tumors. After post-surgery treatment(s), follow-up care begins.

Stage III and IV

The main treatment after surgery for stage III and IV endometrioid cancer is systemic therapy. Either chemotherapy or hormone therapy may be used. Hormone therapy is typically only considered for small or slow-growing endometrioid tumors. In addition to systemic therapy, you may also have EBRT and/or vaginal brachytherapy. After systemic therapy (and radiation, if given), follow-up care begins.

High-risk endometrial cancer

Most endometrial cancers are found early and respond well to treatment. Other, less common types can spread quickly and are harder to treat. At the time of diagnosis, these high-risk endometrial cancers may have already spread beyond the uterus.

High-risk endometrial cancers include:

- Serous carcinoma
- Clear cell carcinoma
- Carcinosarcoma
- Undifferentiated/dedifferentiated carcinoma

Carcinosarcomas appear under the microscope as part endometrial carcinoma and part uterine sarcoma. They are also known as malignant mixed mesodermal tumors or malignant mixed Müllerian tumors (MMMTs).

Like endometrioid tumors, the first sign of high-risk endometrial tumors is vaginal bleeding. However, these kinds of endometrial cancer can also cause the following signs and symptoms:

- Lumps in the pelvis area
- Abnormal Pap smear results
- Fluid buildup or swelling in the abdomen (also known as ascites)

Testing can help determine if the cancer has spread beyond the uterus. If you have not had imaging tests, expect to have them before treatment. Your doctor may also order a cancer antigen 125 (CA-125) blood test. A high level of this substance in the blood may mean that the cancer has spread beyond the uterus. If it

has, CA-125 testing may also be used to see if treatment is working.

For advanced or metastatic serous carcinoma or carcinosarcoma tumors, HER2 testing is also recommended.

The most effective treatment for high-risk endometrial cancers is surgery. A total hysterectomy with BSO is recommended. Surgical staging will be performed to learn the extent of the cancer and assign a stage. When possible, minimally invasive surgery is preferred.

Fertility-sparing therapy is not recommended for these tumor types. If you are not a candidate for surgery, see page 39.

Treatment after surgery

Treatment is almost always needed after surgery for high-risk endometrial cancer. Recommended treatment options depend on the tumor type and stage.

Serous and clear cell carcinoma

If all of the cancer is removed during surgery, no further treatment is needed. Observation is recommended.

For non-invasive stage IA disease, treatment after surgery depends on the results of peritoneal washing ("washings"). Your surgeon will put fluid in the open space of your abdomen and then remove it to see if it has cancer cells. If no cancer cells are found, it is called "negative washings." Treatment with vaginal brachytherapy is one recommended option. If brachytherapy is planned, chemotherapy is sometimes also given. Observation is also an option if the washings are negative.

If the fluid contains cancer cells, it is called "positive washings." Treatment with both

chemotherapy and vaginal brachytherapy is recommended after surgery.

For those with **invasive stage IA, stage IB, or stage II disease**, one option after surgery is chemotherapy. Treatment with EBRT and/or brachytherapy may be added. A second option after surgery for these stages is EBRT. Treatment with brachytherapy may be added.

For those with **stage III or IV serous or clear cell carcinoma**, the main treatment after surgery is chemotherapy. Your doctor may also recommend external radiation and/or brachytherapy in addition to chemotherapy.

The options just described are shown in **Guide 2**.

Carcinosarcoma

For **stage IA** carcinosarcoma, both chemotherapy and vaginal brachytherapy are recommended after surgery. In some cases, EBRT is also given.

For **stages IB, II, III, and IV**, chemotherapy is recommended after surgery. Treatment with external radiation, vaginal brachytherapy, or both may be added.

Regardless of stage, chemotherapy may be started as early as 3 to 6 weeks after surgery.

Guide 2

Serous and clear cell carcinoma: treatment options after surgery

Stage	Treatment options after surgery	Treatments that may be added
Noninvasive stage IA	<p>If negative washings:</p> <ul style="list-style-type: none"> Vaginal brachytherapy <u>or</u> observation <p>If positive washings:</p> <ul style="list-style-type: none"> Chemotherapy <u>and</u> vaginal brachytherapy 	<ul style="list-style-type: none"> Chemotherapy may be added to brachytherapy
<ul style="list-style-type: none"> Invasive stage IA Stage IB Stage II 	<p>Chemotherapy</p> <p>External radiation therapy</p>	<ul style="list-style-type: none"> External radiation Vaginal brachytherapy <ul style="list-style-type: none"> Vaginal brachytherapy
Stages III and IV	Chemotherapy	<ul style="list-style-type: none"> External radiation Vaginal brachytherapy

Brachytherapy can be added to chemotherapy starting at 6 weeks after surgery.

Undifferentiated/dedifferentiated carcinoma

Chemotherapy is recommended after surgery for undifferentiated/dedifferentiated carcinoma. External radiation therapy and/or vaginal brachytherapy may be given in addition to chemotherapy.

Systemic therapy for high-risk endometrial cancer

If chemotherapy is planned after surgery for high-risk endometrial cancer, the preferred regimen is carboplatin and paclitaxel. For stage III or IV HER2-positive serous or carcinosarcoma tumors, a targeted therapy called trastuzumab may be given with chemotherapy.

If you cannot have surgery first

Surgery may not be planned for one or more reasons. It may not be possible to surgically remove the cancer. Or, you may not be able to have surgery because of other health problems. Or, you may not want surgery. In any of these cases, there are two main treatment options for most high-risk endometrial cancers.

The first option is external radiation therapy. Vaginal brachytherapy, chemotherapy, or both may be given in addition to radiation therapy. After treatment, your doctor will check the size of the tumor to see if surgery is possible.

The second option is systemic therapy alone. Chemotherapy is typically given. The goal of systemic therapy is to shrink the tumor enough to be surgically removed. After treatment, your doctor will check the size of the tumor to see if surgery and/or radiation therapy is possible.



share with us.

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

[NCCN.org/patients/comments](https://www.NCCN.org/patients/comments)

When treatment is over

Surveillance begins when there are no signs of cancer after treatment. It is used to find early signs that cancer has returned. See **Guide 3**.

Physical exams

Physical exams are the main method of surveillance for endometrial cancer. Expect to have them on a regular basis. In the first 2 to 3 years after treatment, a physical exam is recommended every 3 to 6 months. Exams are then spaced out to every 6 to 12 months through the fifth year after treatment. After year 5, a physical exam is recommended annually.

Other surveillance testing

If your CA-125 level was high before treatment, it may be measured as part of surveillance testing. Imaging tests are ordered on an as-needed basis after treatment for endometrial cancer. You may need an imaging

test if you develop symptoms or if there is suspicion that the cancer has returned or spread.

Other care

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

Guide 3

Monitoring for the return of endometrial cancer

Physical exams

- **First 2 to 3 years:** exam every 3 to 6 months
- **The next 2 to 3 years (through year 5):** exam every 6 to 12 months
- **After year 5:** exam once a year

Other surveillance testing

- Imaging tests are ordered on an as-needed basis if recurrence is suspected.
- If your CA-125 level was measured and found to be high before treatment, it may be measured as part of surveillance testing.

Recurrence

The return of cancer is called a recurrence or a relapse. If recurrence is suspected based on your symptoms or physical exam findings, imaging tests are needed. You may have one or more of the following imaging tests.

- CT scan of your abdomen, pelvis, and/or chest with contrast
- PET/CT of your whole body
- MRI of your abdomen and pelvis

Treatment for recurrence depends in part on the location of the new cancer growth. After total hysterectomy and BSO, endometrial cancer may return to the vagina. Treatment will depend on whether the cancer is only in the vagina or also in nearby areas or organs.

The treatments you've already had will also be considered. External radiation therapy, for example, is generally not used to treat the same area more than once.

If recurrence is confirmed and biomarker testing has not yet been done, it is recommended at this time.

Biomarkers

Biomarkers are specific features of a cancer. Testing for these features looks for targetable changes to help guide your care. Biomarkers are often mutations (changes) in particular genes. They can also be proteins that are made in response to the cancer.

Biomarker testing is different than genetic testing of the blood for inherited (germline) mutations. Mutations in the tumor or cancer itself are called somatic, acquired, or simply tumor mutations. If any are found, treatment with certain targeted or immunotherapies may be an option. The results of biomarker testing

can also be used to determine whether you meet the criteria for joining certain clinical trials.

Testing for biomarkers involves analyzing a piece of tumor tissue in a lab or testing a sample of blood. Testing for biomarkers may be performed individually, or as part of a larger panel (group). Testing for many biomarkers at one time is called next-generation sequencing (NGS).

Other names for biomarker testing include molecular testing, tumor profiling, genomic testing, tumor gene testing, somatic genomic testing, and mutation testing.

dMMR/MSI-H

All endometrial cancers should be tested for mismatch repair deficiency (dMMR)/high microsatellite instability (MSI-H). If the cancer has this biomarker, you may also be tested for an inherited cancer syndrome called Lynch syndrome. Tumors that are not dMMR/MSI-H are referred to as microsatellite stable (MSS) or mismatch repair proficient (pMMR). See page 14 for more information on this biomarker.

Less common biomarkers

You may also have testing for the less common biomarkers listed below.

- Tumor mutational burden-high (TMB-H)
- NTRK gene fusion

Local recurrence

If endometrial cancer returns to the vagina, pelvis, or abdomen, it is a “local” recurrence. Your treatment options will depend on whether you’ve had radiation therapy at the cancer site. If the cancer site **has not been treated with EBRT**, it is one recommended option. Brachytherapy and/or systemic therapy may be given in addition to EBRT.

Another option for those with no prior external radiation treatment at the recurrence site is exploratory surgery. This involves opening the abdomen to learn how far the cancer has spread and to surgically remove it. If surgery finds that the cancer is only in the vagina or has spread to nearby lymph nodes, EBRT is recommended after surgery. Systemic therapy may be given in addition to EBRT. If the new cancer growth is limited to the vagina, brachytherapy will be considered.

However, if the cancer has spread to the upper abdomen, treatment with systemic therapy is recommended. If the cancer is very small, EBRT may be used in addition to systemic therapy. If there is a significant amount of cancer in the upper abdomen, see *Distant recurrence* on this page.

If the areas of new cancer growth **have been treated with EBRT**, it should not be used again with the goal of curing the cancer. Treatment options may include:

- Exploratory surgery to learn if cancer has spread beyond the vagina and to remove the new cancer growth
- Systemic therapy with or without palliative EBRT (lower-dose EBRT for symptom relief)
- Brachytherapy with or without systemic therapy

Distant recurrence

If endometrial cancer returns after initial 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.

If there are only a few metastases, it may be possible to remove or destroy the tumors using one or more of the local therapies listed below.

- Surgery (if the tumors are small enough)
- EBRT
- Stereotactic body radiation therapy (SBRT) for metastases

Systemic therapy may also be considered if there are only a few metastases.

If there are more than a few new areas of cancer growth, systemic therapy is recommended. Radiation therapy may also be given with the goal of relieving symptoms. This is known as palliative radiation therapy.

At this time, the preferred chemotherapy regimen for recurrent and/or metastatic endometrial cancer is carboplatin and paclitaxel. A targeted therapy called trastuzumab may be added for HER2-positive serous or carcinosarcoma tumors. If you cannot have paclitaxel, docetaxel may be given instead.

If the cancer does not respond or stops responding to first-line systemic therapy, there are other options. If the tumor has certain biomarkers, immunotherapy or targeted therapy may be an option. These newer systemic therapies are generally only considered for cancers that return or spread after chemotherapy and for which there are

no other treatment options. Recommended options are listed next.

Mismatch repair-proficient (pMMR) tumors:

- Lenvatinib (Lenvima) with pembrolizumab (Keytruda)

MSI-H or dMMR tumors:

- Pembrolizumab (Keytruda) (*preferred*)
- Nivolumab (Opdivo)
- Dostarlimab-gxly (Jemperli)
- Avelumab (Bavencio)

TMB-H tumors:

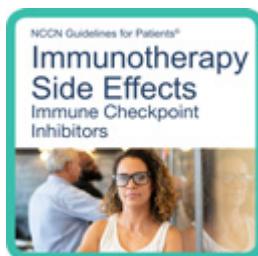
- Pembrolizumab (Keytruda)

NTRK gene fusion-positive tumors:

- Larotrectinib (Vitrakvi)
- Entrectinib (Rozlytrek)

If treatment with immunotherapy is planned, see the *NCCN Guidelines for Patients:*

Immunotherapy Side Effects – Immune Checkpoint Inhibitors at [NCCN.org/patientguidelines](https://www.NCCN.org/patientguidelines) and on the app [NCCN Patient Guides for Cancer](https://www.NCCN.org/patientguidelines/mobile)



Endocrine therapy

Recommended endocrine therapy regimens for recurrent or metastatic endometrial cancer are listed below. Endocrine therapy is typically used for small or slow-growing endometrioid tumors. At this time, preferred regimens include:

- Megestrol acetate (Megace) alternated with tamoxifen
- Everolimus (Afinitor) and letrozole (Femara)

Supportive care

If the cancer progresses during systemic therapy, or if you do not desire cancer treatment, supportive care is an option. Because the cancer cannot be cured, the 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.

Clinical trials

Enrolling in a clinical trial may be an option. 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: Treatments for uterine cancer**.

Key points

- Surgery is the preferred first treatment for most endometrial cancers when possible.

Endometrioid cancer

- Fertility-sparing therapy may be an option for some premenopausal patients with an endometrioid tumor. It involves delaying surgery and having treatment with hormone therapy first.
- Treatment is recommended after surgery for all stage II, III, and IV endometrioid tumors. Some patients with a stage I endometrioid tumor may benefit from treatment after surgery.

High-risk endometrial cancer

- High-risk endometrial tumor types include serous carcinomas, clear cell carcinomas, undifferentiated/differentiated carcinomas, and carcinosarcomas.
- Carcinosarcomas are also known as malignant mixed mesodermal tumors or malignant mixed Müllerian tumors.
- The most effective treatment for high-risk endometrial cancers is surgery. Treatment after surgery is usually needed.

Surveillance

- Follow-up care involves having regular physical exams and staying alert for symptoms of recurrence.

Recurrence

- The return of cancer is called a recurrence or a relapse.
- Treatment for recurrent endometrial cancer depends on the location(s) of the new cancer growth and your treatment history.



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5

Uterine sarcoma treatment

- 46 First steps
- 47 Treatment
- 51 Surveillance
- 52 Recurrence
- 55 Key points

This chapter presents recommended treatment options for a rare type of uterine cancer called uterine sarcoma. Testing, treatment, and follow-up care are explained.

Uterine sarcoma starts in the supporting connective tissues or muscles of the uterus. This type often has a higher chance of spreading and may be harder to treat than endometrial cancer.

Uterine sarcomas differ from endometrial cancer in that they are often found after a hysterectomy. This is because there are limited ways to diagnose uterine sarcomas prior to hysterectomy.

There are different types of uterine sarcomas. The following types are discussed in this book:

- Endometrial stromal sarcoma (ESS)
- Adenosarcoma
- Uterine leiomyosarcoma (uLMS)
- Undifferentiated uterine sarcoma (UUS)
- Perivascular epithelioid cell tumor (PEComa)
- Inflammatory myofibroblastic tumor (IMT)

First steps

Imaging

Imaging tests are needed before starting treatment. A computed tomography (CT) scan of your chest, abdomen, and pelvis (with contrast) is recommended. You may also have magnetic resonance imaging (MRI) of your pelvis, abdomen, or both.

Other imaging tests that may be used to evaluate spread of cancer include combined positron emission tomography (PET)/CT scan of your neck, chest, abdomen, pelvis, and groin. Whether you need other imaging tests will depend on your symptoms and whether your doctor thinks the cancer has spread (metastasized).

Hormone receptor testing

The ovaries make hormones. If the sarcoma is hormone receptor-positive, it means that hormones may help the cancer to grow. Hormone receptor testing helps decide whether the ovaries should be removed. This is decided on a case-by-case basis for those of childbearing age. Hormone receptor testing is typically considered for ESS, uLMS, and adenosarcomas. Testing is performed on either the biopsy sample or on tumor tissue removed during surgery.

Treatment

Treatment of a uterine sarcoma depends on how it was found. They are often found after a hysterectomy. Sometimes pathologists are able to diagnose uterine sarcomas by testing a sample of tissue (a biopsy). But, biopsy is not as reliable for identifying uterine sarcomas as it is for endometrial cancer. This is because sarcomas are often located deep in the muscular wall of the uterus. A third way that a uterine sarcoma may be found is during surgery to remove fibroids. Fibroids are noncancerous tumors that can grow in the uterus and cause symptoms.

In those with a uterus, total hysterectomy and possibly bilateral salpingo-oophorectomy (BSO) is the most effective way to treat a uterine sarcoma. If the cancer cannot be removed with surgery, treatment options include radiation therapy and systemic therapy.

Sarcoma found by biopsy or fibroid removal

Cancer is only in the uterus

If the cancer is only in the uterus, a total hysterectomy is recommended. Your ovaries and fallopian tubes may also be removed (a BSO). This is decided on a case-by-case basis for those of reproductive age. If the cancer is hormone receptor-positive, your doctor is likely to recommend removing them. If you are post-menopausal, a BSO is recommended. If, during surgery, it is discovered that cancer has spread beyond the uterus, you may have more surgery to remove it. This decision is also made on a case-by-case basis. See *Treatment after surgery* on the next page.

Possible spread beyond the uterus

If the cancer has (or may have) spread beyond the uterus, surgery will be considered. Your surgeon will consider the extent of the cancer, your symptoms, and how well the cancer can be removed with surgery. If surgery is planned, a total hysterectomy is recommended. The cancer that has spread beyond the uterus will also be removed if possible. Your ovaries and fallopian tubes may also be removed. This is decided on a case-by-case basis for those of reproductive age. If the cancer is hormone receptor positive, your doctor is likely to recommend removing them. See *Treatment after surgery* on the next page.

Having surgery first is not an option

If you don't want or can't have surgery, treatment with systemic therapy, palliative external radiation therapy, or both is recommended. Brachytherapy may be used in addition to one or both of these treatments.

Chemotherapy is often given first for systemic therapy. For tumors with certain biomarkers, other systemic therapy that targets the biomarker may be given instead. Recommended first-line systemic therapy options for inoperable sarcomas are listed in **Guide 5** on page 50.

Sarcoma found during prior hysterectomy

If the cancer was found after a partial or total hysterectomy, treatment will depend on the results of the original hysterectomy and whether the ovaries and fallopian tubes were removed.

If the tumor was not removed in one piece or if the cervix was not removed, you may have another surgery to remove the cancer and the remaining cervix.

If your ovaries and fallopian tubes were not removed during surgery, they may be removed now. If only one ovary and its fallopian tube were initially removed, the remaining ovary and fallopian tube may be removed. This may be the best choice for low-grade ESS tumors, adenosarcomas, and estrogen receptor-positive tumors.

Treatment after surgery

Treatment after surgery depends on the tumor type.

Low-grade ESS or low-risk adenosarcoma

If you still have your ovaries and fallopian tubes, surgery to remove them (a BSO) is recommended for **stage I** tumors. If you've already had a BSO, or if you are menopausal, observation (no treatment) is recommended.

A BSO is also recommended for **stage II, III, IVA, and IVB** low-grade ESS tumors and low-risk adenosarcomas. In addition to surgery, one or both of the following treatments may be given:

- Anti-estrogen hormone therapy
- External radiation therapy

Aromatase inhibitors are the preferred anti-estrogen therapy for low-grade ESS and low-risk adenosarcomas. All of the recommended options for anti-estrogen therapy are listed in **Guide 4**.

If radiation therapy is used for stage IVB cancer, it is considered palliative. This means the goal is not to treat the cancer, but to control or prevent symptoms caused by the tumor.

Guide 4

Anti-estrogen therapy for low-grade ESS, low-risk adenosarcoma, or hormone receptor-positive uterine sarcomas

- Aromatase inhibitors (**preferred for low-grade ESS and low-risk adenosarcoma**)
- Fulvestrant
- Megestrol acetate
- Medroxyprogesterone acetate
- GnRH analogs (for those with at least one functional ovary)

High-risk adenosarcoma

If you still have your ovaries and fallopian tubes, surgery to remove them (a BSO) is recommended for **stage I** high-risk adenosarcomas. If you've already had a BSO, or if you are menopausal, observation (no treatment) is recommended.

A BSO is also recommended for **stage II, III, IVA, and IVB** high-risk adenosarcomas. Your doctor will consider treatment with systemic therapy after surgery. Either a chemotherapy or a targeted therapy drug is often given. Or, if the cancer is hormone receptor-positive, your doctor may recommend anti-estrogen therapy.

If systemic therapy is planned, palliative external radiation therapy may also be added.

Other tumor types

The information that follows applies to the following tumor types:

- High-grade ESS
- uLMS
- UUS
- Other sarcomas, such as PEComa
- Inflammatory myofibroblastic tumor (IMT)

The recommended treatment after surgery for these tumor types is presented according to stage.

If the cancer is **stage I**, no further treatment is needed after surgery. The cancer will be observed. You can start surveillance and follow-up care.

For **stage II and III** cancers, some people have more treatment after surgery. Your doctor will consider treatment with systemic therapy and/or external radiation therapy. If the results of surgery are very good, observation (no treatment) may be an option.

If the cancer is **stage IV**, more treatment is needed after surgery. Systemic therapy, external radiation therapy, or both are recommended for stage IVA disease. For stage IVB, the main treatment is systemic therapy. Palliative radiation therapy may be used to prevent or control symptoms caused by the cancer.

If systemic therapy is needed, either a chemotherapy or a targeted therapy drug is often given. Or, if the cancer is hormone receptor-positive, your doctor may recommend anti-estrogen therapy.

About systemic therapy after surgery

The systemic therapy most often given after surgery is chemotherapy. If treatment with chemotherapy is planned, there are several preferred regimens. Most include doxorubicin (Adriamycin). Your doctor will consider several factors when recommending a chemotherapy regimen. **See Guide 5.**

If the cancer has certain biomarkers (features), targeted therapy with a tyrosine kinase inhibitor (TKI) may be a better choice than chemotherapy. A small number of uterine sarcomas have a biomarker (feature) called *NTRK* gene fusion. TKI therapy will be considered after surgery for these cancers. It will also be considered for inflammatory myofibroblastic tumors (IMTs) with *ALK* translocation.

Guide 5

First-line drug therapy for advanced, recurrent/metastatic, or inoperable uterine sarcomas

Preferred regimens

- Doxorubicin
- Docetaxel + gemcitabine
- Doxorubicin + ifosfamide
- Doxorubicin + dacarbazine
- Doxorubicin + trabectedin (for uLMS)

Regimens that may be used in certain cases

For *NTRK* gene fusion-positive tumors:

- Larotrectinib (Vitrakvi) or entrectinib (Rozlytrek)

For inflammatory myofibroblastic tumors (IMTs) with *ALK* translocation:

- Crizotinib (Xalkori)
- Ceritinib (Zykadia)
- Brigatinib (Alunbrig)
- Lorlatinib (Lorbrena)
- Alectinib (Alecensa)

For PEComas:

- Albumin-bound sirolimus

Surveillance

Surveillance begins when there are no signs of cancer after treatment. It is used to find early signs that cancer has returned. Physical exams and imaging tests are used to monitor for the return of uterine sarcomas. **See Guide 6.**

You may have additional imaging tests not listed in Guide 6 if:

- You develop symptoms
- Your doctor suspects the cancer may have metastasized
- There are abnormal physical exam findings

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

Guide 6 Monitoring for the return of uterine sarcoma

Physical exams

- **First 2 to 3 years:** exam every 3 to 4 months
- **After that:** exam once or twice a year

Recommended:

CT scan of chest, abdomen, and pelvis with contrast

Optional:

MRI of abdomen and pelvis and chest CT without contrast

- **First 3 years:** imaging every 3 to 6 months
- **Years 4 and 5:** imaging every 6 to 12 months

You may have imaging every 1 to 2 years for up to 5 more years. Your doctor will decide whether imaging should continue based on the features of your cancer (tumor type, stage, grade)

Recurrence

The return of cancer after a cancer-free period is known as a recurrence. If recurrence is suspected, you will likely have imaging tests. If there is suspicion that the cancer has spread to areas far from the pelvis (metastasized), imaging may include a PET/CT scan of your neck, chest, abdomen, pelvis, and groin.

Treating a recurrence depends in part on the location of the new cancer growth. After surgery to remove the uterus, ovaries, and fallopian tubes, cancer may return to the vagina, to areas near the vagina, or to areas far from the pelvis.

Treatment of recurrent uterine sarcoma also depends on whether you've had external beam radiation therapy (EBRT). EBRT is generally not used to treat the same area more than once, so this is important when deciding how to treat recurrent cancer.

Cancer returned to the vagina or pelvis

Prior external radiation

If you received prior treatment with EBRT, one of the following approaches may be used to treat cancer that returns to the vagina or pelvis:

- Surgery, with or without systemic therapy
- Systemic therapy
- Careful re-treatment of selected areas using EBRT
- Brachytherapy, with or without EBRT of selected areas

If systemic therapy is planned (alone or in addition to surgery), anti-estrogen hormone therapy is preferred for low-grade ESS and low-risk adenosarcoma.

No prior external radiation

If you have not had EBRT, options for treating uterine sarcoma that returns to the pelvis include surgery and EBRT.

If surgery is planned, you may have EBRT with or without systemic therapy first to try to shrink the tumor. If all of the cancer is not removed during surgery, EBRT may be used after surgery to treat residual areas of cancer. It will not be used again, however, if it was used before surgery. If used after surgery, brachytherapy and/or systemic therapy may be given in addition to EBRT.

If treatment with EBRT is planned instead of surgery, brachytherapy and/or systemic therapy may also be used. For low-grade ESS and low-risk adenosarcoma, anti-estrogen hormone therapy is preferred for systemic therapy.

Distant recurrence

If uterine sarcoma returns and spreads to 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.

Biomarker testing

If biomarker testing has not yet been done, it is recommended at this time. Biomarkers are targetable features of a cancer. They are often mutations (changes) in particular genes. Testing for these mutations helps guide treatment for recurrent, metastatic uterine sarcoma. The results can also be used to determine whether you meet the criteria for joining certain clinical trials.

Testing for biomarkers involves analyzing a piece of tumor tissue in a lab or testing a sample of blood. Testing for the following biomarkers is recommended:

- Microsatellite instability (MSI)
- Tumor mutational burden-high (TMB-H)
- *NTRK* gene fusion
- IMT with *ALK* rearrangement

An inflammatory myofibroblastic tumor (IMT) is a rare type of uterine sarcoma. Most IMTs have a biomarker called *ALK* translocation or rearrangement. Cancers with this biomarker are referred to as ALK-positive or ALK+.

Testing for biomarkers may be performed individually, or as part of a larger panel (group). Testing for many biomarkers at one time is called next-generation sequencing (NGS). NGS may find other gene mutations for which targeted treatments may be available.

Minimal metastases

If there are only a few metastases, removing or destroying them with surgery or ablative therapies may be an option. Ablative therapies include image-guided ablation and stereotactic body radiation therapy (SBRT). Ablation destroys cancer cells using heat, cold, or light-activated drugs. SBRT is a highly specialized type of external radiation requiring 5 or fewer treatment sessions.

If surgery is possible, systemic therapy and/or EBRT may be used after surgery to kill any remaining cancer cells. If the metastases cannot be surgically removed, treatment with systemic therapy and/or local therapies is recommended. Local therapies include EBRT and ablation. If systemic therapy works well, surgery may become an option.

Widespread metastases

If there are many new areas of cancer growth outside the pelvis, systemic therapy is recommended. Chemotherapy is usually given first for recurrent, metastatic disease. There are several preferred first-line regimens. Most include doxorubicin (Adriamycin). **See Guide 5.**

If the cancer has certain biomarkers, targeted therapy with a tyrosine kinase inhibitor (TKI) may be a better choice than chemotherapy. A small number of uterine sarcomas have a biomarker called *NTRK* gene fusion. TKI therapy will be considered for these cancers. It will also be considered for IMTs with *ALK* translocation.

Palliative EBRT may be used in addition to systemic therapy. The goal is to shrink the tumor(s) in order to relieve or prevent symptoms. An alternative to having any treatment at this stage is to begin supportive (also called palliative) care.

Because the cancer cannot be cured, the 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, improve your eating, and help you feel better overall. When used for advanced cancers, supportive care is often called palliative care.

Enrolling in a clinical trial may also be an option. 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: Treatments for uterine cancer.**

Second-line and beyond systemic therapy

If the cancer does not respond or stops responding to first-line systemic therapy, there are other options. Other first-line regimens in **Guide 5** can be tried. Otherwise, regimens that can be tried next (second-line regimens) are listed in **Guide 7**. If the tumor has certain biomarkers, immunotherapy or targeted therapy may be an option.

Guide 7

Second-line or after systemic therapy for advanced, recurrent/metastatic, or inoperable disease

Recommended regimens

- Trabectedin (only for uLMS)
- Gemcitabine + dacarbazine
- Gemcitabine + vinorelbine
- Dacarbazine
- Gemcitabine
- Epirubicin
- Ifosfamide
- Liposomal doxorubicin
- Pazopanib
- Temozolomide
- Eribulin

Regimens that may be used in certain cases

For PEComas:

- Sirolimus
- Everolimus
- Temsirolimus

For TMB-H tumors:

- Pembrolizumab

For *BRCA2*-altered uLMS:

- Olaparib
- Rucaparib
- Niraparib

Key points

- Uterine sarcomas are rare. They start in the wall or muscles of the uterus.
- Uterine sarcomas can spread quickly and be hard to treat. They are often found after a hysterectomy done for other reasons or during surgery to remove fibroids.

Testing

- Imaging tests are needed before starting treatment. A CT scan of your chest, abdomen, and pelvis with contrast is recommended. You may also have MRI of your pelvis, abdomen, or both.
- If these tests are unclear, a PET/CT scan may be ordered. Other imaging is individualized.
- Hormone receptor testing will be considered for ESS, uLMS, and adenosarcomas. This helps decide whether the ovaries should be removed for those of childbearing age.

Sarcoma found by biopsy or fibroid removal

- Total hysterectomy is recommended when possible. The decision to do a BSO is individualized for those of reproductive age. BSO is often recommended if the cancer is hormone receptor-positive.
- If you don't want or can't have surgery, treatment with systemic therapy, external radiation therapy, or both is recommended.

Sarcoma found during prior hysterectomy

- If the tumor was not removed in one piece or if the cervix was not removed, you may have another surgery to remove the cancer and the remaining cervix.
- If your ovaries and fallopian tubes were not removed during hysterectomy, they may be removed now. This may be the best choice for low-grade ESS, adenosarcoma, or estrogen receptor-positive tumors.

Surveillance

- Physical exams are recommended every 3 to 4 months in the first 2 to 3 years after treatment. After that, exams are performed once or twice a year.
- Imaging is recommended every 3 to 6 months for the first 3 years after treatment. During years 4 and 5, imaging is recommended every 6 to 12 months.
- You may have imaging every 1 to 2 years for up to 5 more years. This is individualized.

Recurrence

- After a hysterectomy and BSO, cancer may return to the vagina, to areas near the vagina, or to areas far from the pelvis.
- Treatment for recurrence depends on the location of the new cancer growth and whether you've had external radiation therapy.

6

Survivorship

- 57 Staying alert for recurrence or spread
- 58 Early, late, and long-term effects
- 60 Healthy habits
- 61 More information

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 a key 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, ask your oncologist for 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

Staying alert for recurrence or spread

Your cancer treatment team and your PCP will work together to make sure you get recommended follow-up testing. But, you will also have a job—paying close attention to your body.

Some kinds of cancer can return without giving your body any hints. If uterine cancer does come back, it often affects your body in ways that you can feel or notice (symptoms). Your doctor will teach you about the symptoms that may mean uterine cancer has returned or spread. They include:

- Vaginal bleeding
- Blood in your urine or stool
- Loss of appetite
- Weight loss
- Pain in your stomach, midsection, hip, or back
- Cough
- Shortness of breath
- Swelling in your stomach area or legs

If you notice any of these symptoms, contact your doctor right away. Do not wait until your next scheduled visit.

Early, late, and long-term effects

Some side effects of uterine cancer treatment can start early and linger longer than expected. Others may not appear until long after treatment is over. Many uterine cancer survivors experience changes in bowel, urinary, and sexual function.

Premature menopause

If you have not entered menopause, surgery that removes both ovaries (or whole pelvic radiation therapy) will cause it. This is known as surgical menopause. It is caused by the sudden drop in estrogen in the body. This drop can cause symptoms of menopause, including:

- Hot flashes
- Sleeping problems
- Night sweats
- Weight gain
- Changes in mood
- Thinning, drying, and irritation of the vaginal lining (vaginal atrophy)

When caused by surgery, the symptoms of menopause may be sudden and more severe. There are also long-term risks of not having enough estrogen. They include heart or blood vessel problems (cardiovascular disease) and bone loss (osteoporosis).

Hormone replacement therapy

If you have symptoms of surgical menopause, your doctor may suggest hormone replacement therapy (HRT). One option is systemic HRT. Estrogen is given as a pill taken by mouth or a patch placed on the skin. Another option for HRT is vaginal estrogen cream or tablets. This type may be the best

option for symptoms that mainly affect the vagina, such as dryness. Discussion with a menopausal symptom team is recommended to determine whether this treatment is right for you.

Bowel and bladder changes

After surgery or radiation therapy for uterine cancer, it may be harder to hold urine in your bladder. This is called urinary incontinence. You may also experience urgency—a sudden and strong need to urinate. Watery and/or frequent bowel movements (diarrhea) are also possible.

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, as 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 who 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.

Sexual and vaginal wellness

You may have sexual side effects after uterine cancer treatment, including:

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

Vaginal moisturizers

Older age, menopause, and some uterine cancer treatments can cause the vagina to become dry and less stretchy. To offset this side effect, use of water-based vaginal moisturizers is encouraged. Vaginal moisturizers restore moisture to the vagina and help to keep the vaginal tissue healthy. They can be used daily, and many come with applicators to make using them easier.

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 may help. 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.

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.

Other physical side effects

In addition to effects on bowel, bladder, and sexual function, more general effects such as fatigue, trouble breathing, and difficulty sleeping are common.

Radiation treatment to the pelvis can weaken bones in the pelvis. This puts you at increased risk of fractures. Your doctor may 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 uterine 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 uterine cancer survivors.

Ask your treatment team for a complete list of possible late and long-term side effects.

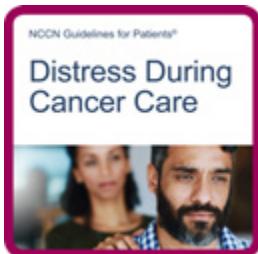
Mental health

The effects of uterine 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.

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.

For more information, see the *NCCN Guidelines for Patients: Distress During Cancer Care* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the app [NCCN Patient Guides for Cancer](#)



Healthy habits

Monitoring for the return of uterine 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.

Cancer screening

Get screened for other types of cancer, such as breast, skin, and colorectal cancer. Your primary care doctor can tell you the recommended screening tests based on your age and risk level. If your cervix and/or ovaries were not removed as part of treatment, ask your doctor about screening for these cancer types.

Other health care

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

Diet and exercise

Leading a healthy lifestyle includes maintaining a healthy body weight. Try to exercise at a moderate intensity for at least 150 minutes per week. All patients should have a discussion with their doctor before starting a new exercise regimen.

Eat a healthy diet with lots of plant-based foods. Alcohol may increase the risk of certain cancers. Drink little to no alcohol.

Quit smoking

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 are available at

[NCCN.org/patientguidelines](https://www.NCCN.org/patientguidelines) and on the app NCCN Patient Guides for Cancer:

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

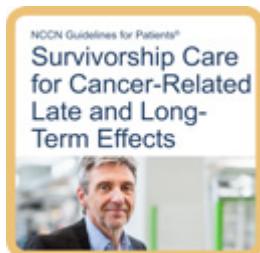
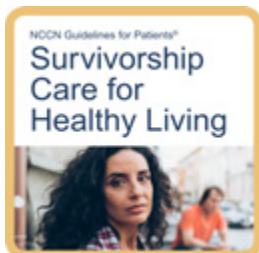
These resources address topics relevant to survivors of uterine cancer, including:

- Anxiety, depression, and distress
- Fatigue
- Pain
- Sexual problems
- Sleep problems
- Healthy lifestyles
- Immunizations
- Employment, insurance, and disability



Do I need a second opinion?

Uterine cancer is a serious diagnosis. Consider having an in-person meeting with a different doctor to see if they are in agreement with your diagnosis and treatment plan. More information on seeking a second opinion is provided in the next chapter.



7

Making treatment decisions

63 It's your choice

63 Questions to ask

69 Resources

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

It's your choice

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

Treatment decisions are very personal. What is important to you may not be important to someone else. Some things that may play a role in your decision-making:

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

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with

your team, it will help you feel supported when considering options and making treatment decisions.

Second 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 cancer care provider review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

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

Support groups

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

Questions to ask

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

Questions about cancer testing

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

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

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

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

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

American Association for Cancer Research (AACR)
aacr.org

American Cancer Society (ACS)
cancer.org/cancer/endometrial-cancer.html
cancer.org/cancer/uterine-sarcoma.html

CancerCare
cancercare.org

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

Cancer Support Community
cancersupportcommunity.org

ECANA: Endometrial Cancer Action Network for African-Americans
ecanawomen.org

FORCE: Facing Our Risk of Cancer Empowered
facingourrisk.org

Foundation for Women's Cancer
foundationforwomenscancer.org

Go Girls
gogirlssupport.org

GOG Foundation
gog.org

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

National Coalition for Cancer Survivorship
canceradvocacy.org

NCCN Patient and Caregiver Resources
nccn.org/patientresources

NRG Oncology
nrgoncology.org

Ovarian Cancer Research Alliance (OCRA)
ocrahope.org

PAN Foundation
panfoundation.org

SHARE
sharecancersupport.org

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



Words to know

abdomen

The belly area between the chest and pelvis.

adenocarcinoma

Cancer of cells that line organs and make fluids. Most endometrial cancers are adenocarcinomas.

ascites

Abnormal fluid buildup in the belly (abdomen) or pelvis.

biopsy

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

bilateral salpingo-oophorectomy (BSO)

Surgery to remove both ovaries and both fallopian tubes.

brachytherapy

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

cancer antigen 125 (CA-125)

A high level of this substance in blood may mean that endometrial cancer has spread beyond the uterus.

cancer grade

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

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

carcinosarcoma

A high-risk type of endometrial cancer. Also known as malignant mixed Müllerian tumor (MMMT).

cervix

The lower part of the uterus that connects to the vagina (birth canal).

clear cell carcinoma

A high-risk type of endometrial cancer.

clinical trial

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

computed tomography (CT)

An imaging test that uses x-rays from many angles to make a picture of areas inside of the body.

contrast

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

debulking

Surgery to remove as much cancer as possible. Also called cytoreductive surgery.

endocrine therapy

Treatment that stops the making or action of hormones in the body. Also called hormone therapy.

endometrioid cancer

The most common type of endometrial cancer.

endometrium

The layer of tissue that lines the uterus.

external beam radiation therapy (EBRT)

A cancer treatment with radiation received from a machine outside the body.

fallopian tube

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

genetic counselor

A health expert who has special training to help patients understand changes in genes that are related to disease.

gynecologic oncologist

A surgeon who is an expert in cancers that start in the female reproductive organs. Many gynecologic oncologists are also medical oncologists.

human epidermal growth factor receptor 2 (HER2)

A protein involved in normal cell growth. May be made in larger than normal amounts by some types of cancer cells. This may cause the cancer to grow more quickly.

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 special disease-fighting cells located throughout the body.

Lynch syndrome

Abnormal changes within genes that increase the chances of developing colon, rectal, endometrial, ovarian, and other cancers. It is also called hereditary nonpolyposis colorectal cancer (HNPCC) syndrome.

medical oncologist

A doctor who is an expert in treating cancer with drugs such as chemotherapy. Many medical oncologists specialize in specific

cancers, such as gynecologic cancers or sarcomas.

menopause

The time of life when the ovaries stop producing hormones and menstrual periods stop.

metastasis

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

microscopic metastases

Cancer cells that have spread from the first tumor to another body part and are too small to be seen with the naked eye.

neuropathy

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

observation

A period of watching and waiting for cancer growth or recurrence.

ovary

One of a pair of organs that make eggs for reproduction and make hormones.

pathologist

A doctor who is an expert in evaluating cells and tissues to diagnose disease.

pelvic exam

A physical exam of the vagina, cervix, uterus, fallopian tubes, and ovaries.

pelvis

The body area between the hip bones.

peritoneal cavity

The space inside the belly (abdomen) that contains abdominal organs such as the intestines, stomach, and liver.

Words to know

peritoneal washing

A test in which a special liquid is used to wash the inside of the belly (peritoneal cavity) to check for cancer cells.

peritoneum

The layer of tissue that lines the inside of the belly (abdomen) and pelvis and covers most organs in this space.

platinum-based chemotherapy

Treatment with two or more chemotherapy drugs and the main drug is made with platinum. Such drugs include cisplatin and carboplatin.

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.

radiologist

A doctor who is an expert in interpreting imaging tests.

recurrence

The return of cancer after treatment. Also called relapse.

regimen

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

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.

serous carcinoma

A high-risk type of endometrial cancer.

supportive care

Care given to improve the quality of life of people with cancer. Helps prevent or relieve

symptoms caused by the cancer or cancer treatment. Also called palliative care.

surgical menopause

The stopping of menstrual periods caused by surgery to remove the ovaries.

surgical staging

The process of determining the stage (extent) of the cancer during surgery to remove the cancer.

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.

undifferentiated/dedifferentiated carcinoma

A high-risk type of endometrial cancer.

unilateral salpingo-oophorectomy (USO)

Surgery that removes one ovary and the attached fallopian tube.

uterus

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

vagina

The muscular tube through which babies are born.

washings

Sample of liquid that is tested for cancer cells after it is used to “wash” the inside of the belly (peritoneal cavity).

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms, Version 1.2023 . It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

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

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.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
Duarte, California
800.826.4673 • cityofhope.org

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

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

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

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

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

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

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

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

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

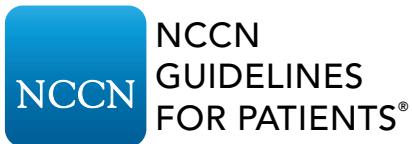
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

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

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Uterine Cancer

Endometrial Cancer

Uterine Sarcoma

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