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Treating Uterine Sarcoma

If you've been diagnosed with uterine sarcoma, your cancer care team will discuss your treatment options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is uterine sarcoma treated?

These are some common treatment options for women with uterine sarcoma:

- Surgery for Uterine Sarcomas
- Radiation Therapy for Uterine Sarcomas
- Chemotherapy for Uterine Sarcomas
- Hormone Therapy for Uterine Sarcomas
- Targeted Drug Therapy for Uterine Sarcomas
- Immunotherapy for Uterine Sarcomas

Common treatment approaches

A combination of treatments may be used to treat uterine sarcoma. The choice of treatment depends largely on thetype and stage of your cancer. Other factors might include your age, your overall health, whether you plan to have children, and your personal preferences.

When possible, most women with uterine sarcoma have surgery to remove the cancer. Radiation, chemotherapy, and hormone therapy are sometimes used to help lower the risk of the cancer coming back after surgery. These treatments may also be used for cancers that cannot be removed with surgery or when a woman can't have surgery because she has other health problems.

Treatment for Uterine Sarcoma, by Type and Stage

Who treats uterine sarcoma?

Depending on your situation, you may have different types of doctors on your treatment team:

- A gynecologist: a doctor who specializes in diseases of the female reproductive tract
- A gynecologic oncologist: a doctor who specializes in the treatment of cancers of the female reproductive system (including surgery, chemotherapy, targeted drug therapy, hormone therapy, and other medicines to treat cancer)
- A radiation oncologist: a doctor who uses radiation to treat cancer
- A **medical oncologist:** a doctor who uses chemotherapy, targeted drug therapy, hormone therapy, immunotherapy, and other medicines to treat cancer

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

• Health Professionals Associated with Cancer Care

Making treatment decisions

It's important to discuss all of your treatment options as well as their possible side effects with your family and your treatment team to make the choice that best fits your needs. If there's anything you don't understand, ask to have it explained.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- Questions to Ask About Uterine Sarcoma
- Seeking a Second Opinion

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-

the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

Clinical Trials

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

Complementary and Integrative Medicine

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors and you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Surgery for Uterine Sarcomas

- Total hysterectomy
- Radical hysterectomy
- Bilateral salpingo-oophorectomy (BSO)
- Lymph node surgery

- Other procedures that may be done during surgery
- Sexual impact of surgery
- More information about Surgery

Surgery is the main treatment for early stage <u>uterine sarcoma</u>¹. The goal of surgery is to remove all of the cancer in one procedure, and if possible in one piece. This usually means removing the entire uterus with the cervix (total hysterectomy). In some cases, the fallopian tubes, ovaries, and part of the vagina may also need to be removed. Some lymph nodes or other tissue may be taken out as well to see if the cancer has spread outside the uterus. What's done depends on the <u>type</u>² and grade of the cancer and how far it has spread. (See <u>How Is Uterine Sarcoma Staged?</u>³) The patient's overall health and age are also important factors.

In some cases, <u>tests done before surgery</u>⁴ let the doctor plan the operation ahead of time. These tests include imaging studies, like ultrasound, CT scan, or MRI, as well as a pelvic exam, endometrial biopsy, and/or D&C. In other cases, the surgeon has to decide what needs to be done based on what they find during surgery. For example, sometimes there's no way to know for sure that a tumor is cancer until it's removed during surgery.

Total hysterectomy

This surgery removes the whole uterus (the body of the uterus and the cervix). The loose connective tissue around the uterus (called the **parametrium**), the tissue connecting the uterus and sacrum (the uterosacral ligaments), and the vagina are not removed. Removing the ovaries and fallopian tubes is not part of a hysterectomy --- officially it's a separate procedure known as a **bilateral salpingo-oophorectomy** (**BSO**). The BSO is often done along with a hysterectomy in the same operation (see below).

If the uterus is removed through an incision (cut) in the front of the abdomen (belly), the surgery is called an **abdominal hysterectomy**. When the uterus is removed through the vagina, it's called a **vaginalhysterectomy**. When it is removed through small incisions on the belly using alaparoscope it is called a **laparoscopic hysterectomy**. A laparoscope is a thin lighted tube with a video camera at the end. It can be put into the body through a small incision in the abdomen and lets the doctor see inside the body without making a big incision. The doctor can use long, thin tools that are put in through other small incisions to operate. A laparoscope is sometimes used to help remove the uterus when the doctor is doing a vaginal hysterectomy. This is called a **laparoscopic assisted vaginal hysterectomy**. The uterus can also be removed through the

abdomen with a laparoscope, sometimes with a robotic approach, in which the surgeon sits at a control panel in the operating room and moves robot arms to operate. Laparoscopic procedures have shorter recovery times than abdominal hysterectomies, but are not possible to all patients. Talk with your surgeon about how the surgery will be done and why it's the best plan for you.

If <u>lymph nodes</u>⁵ or other organs need to be seen, removed, or tested, this can be done through the same incision as the abdominal hysterectomy or laparoscopic hysterectomy. If a hysterectomy is done through the vagina, lymph nodes can be removed after the hysterectomy by using a laparoscope.

Either general or regional anesthesia is used for the procedure. This means that the patient is in a deep sleep or is sedated and numb from the waist down.

For an abdominal hysterectomy the hospital stay is usually 3 to 5 days. Complete recovery takes about 4 to 6 weeks. Someone who gets a laparoscopic procedure or vaginal hysterectomy can usually go home the same day as the surgery and recovery often takes 2 to 3 weeks.

After a hysterectomy, a woman cannot become pregnant and give birth to children. Surgical complications are rare but could include bleeding, wound infection, and damage to the urinary (bladder and/or ureters) or bowel systems.

Radical hysterectomy

This operation removes the entire uterus as well as the tissues next to the uterus and cervix (parametrium and uterosacral ligaments) and the upper part of the vagina (near the cervix). This operation is not often used for uterine sarcomas, but may be needed if the tumor appears to have spread to the nearby tissues.

Radical hysterectomy is most often done through an abdominal surgical incision or with a laparoscope, with or without a robotic approach (in which the surgeon sits at a control panel in the operating room and moves robot arms to operate) but it can also be done through the vagina. Most people having a radical hysterectomy also have some lymph nodes removed, either through the abdominal incision or with a laparoscope. A radical hysterectomy is done using general anesthesia.

Because more tissue is removed by a radical hysterectomy than with a total hysterectomy, the hospital stay might be longer.

After this surgery, a person cannot become pregnant and give birth to children.

Complications associated with a radical hysterectomy can include bleeding, wound infection, and damage to the urinary (bladder and/or ureters) or bowel systems. If some of the nerves of the bladder are damaged, a catheter is often needed to empty the bladder for some time after surgery. This usually gets better with time and the catheter can be taken out later.

Bilateral salpingo-oophorectomy (BSO)

This operation removes both fallopian tubes and both ovaries. In treating uterine sarcomas, this operation is usually done at the same time the uterus is removed. If both of your ovaries are removed, you will go into menopause if you have not done so already.

Lymph node surgery

Sometimes during surgery it looks like the cancer might have spread outside the uterus or nearby lymph nodes look swollen on imaging tests. In this case, your surgeon might do a **lymph node dissection**or a**lymph node sampling,** which removes lymph nodes in the pelvis and/or those around the aorta (the main artery that runs from the heart down along the back of the abdomen and pelvis). These lymph nodes are then checked in the lab to see if they have cancer cells. If cancer is found in the lymph nodes, it means that the cancer has already spread outside the uterus. Cancer in the lymph nodes is often associated with a poorer prognosis (outlook).

This operation is done through the same surgical incision in the abdomen as the abdominal hysterectomy or laparoscopic hysterectomy. If a vaginal hysterectomy has been done, the lymph nodes can be removed with laparoscopic surgery.

While some people might have their lymph nodes removed during surgery for uterine sarcoma, it is still not known if this improves their outlook (unless the nodes have cancer cells in them). Studies are being done to help answer this question.

A side effect of removing lymph nodes in the pelvis can lead to a build-up of fluid in the legs, called **lymphedema**. This is more likely if radiation is given after surgery. You can find out more about this in <u>Lymphedema</u>.⁶

Other procedures that may be done during surgery

 Omentectomy: The omentum is a layer of fatty tissue that covers the abdominal contents like an apron. Cancer sometimes spreads to this tissue. When this tissue is removed, its called an **omentectomy**. The omentum is sometimes removed at the same time the hysterectomy is done if cancer has spread there, or as a part of staging⁷.

- Peritoneal biopsies: The tissue lining the pelvis and abdomen is called theperitoneum. Peritoneal biopsies remove small pieces of this lining to check for cancer cells.
- **Pelvic washings:** In this procedure, the surgeon "washes" the abdominal and pelvic cavities with salt water (saline), collects it, and then sends the fluid to the lab to see if it s has cancer cells.
- Tumor debulking: If cancer has spread throughout the abdomen, the surgeon may attempt to remove as much of the tumor as possible. This is called debulking. For some types of cancer, debulking can help other treatments (like radiation or chemotherapy) work better.

Sexual impact of surgery

If you are premenopausal, removing your uterus stops menstrual bleeding (periods). If your ovaries are also removed, you will go into menopause. This can lead to vaginal dryness and pain during sex. These symptoms can be improved with non-hormonal treatments or in some cases, estrogen treatment. Estrogen treatment isn't safe for all women with uterine sarcoma.

While physical and emotional changes can affect the desire for sex, these surgical procedures do not prevent a woman from feeling sexual pleasure. A woman does not need ovaries or a uterus to have sex or reach orgasm. Surgery can actually improve a woman's sex life if the cancer had caused problems with pain or bleeding during sex. See Sex and the Adult Female with Cancer⁸ for more on this.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer Surgery</u>⁹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>¹⁰.

Hyperlinks

- 1. www.cancer.org/cancer/types/uterine-sarcoma/about/what-is-uterine-sarcoma.html
- 2. www.cancer.org/cancer/types/uterine-sarcoma/about/what-is-uterine-sarcoma.html
- 3. <u>www.cancer.org/cancer/types/uterine-sarcoma/detection-diagnosis-staging/staging.html</u>
- 4. <u>www.cancer.org/cancer/types/uterine-sarcoma/detection-diagnosis-staging/how-diagnosed.html</u>
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- 6. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
- 7. <u>www.cancer.org/cancer/types/uterine-sarcoma/detection-diagnosis-staging/staging.html</u>
- 8. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-women-with-cancer.html</u>
- 9. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
- 10. www.cancer.org/cancer/managing-cancer/side-effects.html

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Radiation Therapy for Uterine Sarcomas

- Types of radiation therapy
- Side effects of radiation therapy
- More information about radiation therapy

Radiation therapy uses high-energy x-rays or particles to destroy cancer cells or slow their growth.

Radiation might be used to treat uterine sarcoma in these ways:

- After surgery (adjuvant radiation) it may help lower the chance of the cancer coming back in the pelvis. It might be done for cancers that are high grade or when cancer cells are found in the lymph nodes. The entire pelvis or part of the pelvis may be treated with external beam radiation therapy (see below). Sometimes the radiation field will also include an area of the abdomen (belly) called the paraaortic field. This is the area around the aorta (the main artery). Brachytherapy (internal radiation) may also be used in some cases after surgery (see below).
- It might be used alone or with chemo as the main treatment if surgery can't be done because of other health problems.
- It might be used to treat **problems caused by tumor growth**, but is not intended to cure the cancer. For instance, radiation can be used to shrink a tumor that's causing pain and swelling by pressing on nearby nerves and blood vessels. This is called <u>supportive or palliative care</u>¹.

Radiation therapy seems to help keep some uterine sarcomas from coming back after surgery, but there is not enough information to know if it can help someone live longer.

Types of radiation therapy

Two types of radiation treatments might used for uterine sarcoma:

- External beam radiation therapy
- Internal radiation therapy or brachytherapy

Sometimes brachytherapy and external beam radiation therapy are used together. How much of the pelvis needs to be exposed to radiation therapy and the type(s) of radiation used depend on the extent of the disease.

External beam radiation therapy

External beam radiation therapy (EBRT)² is the more common type of treatment for uterine sarcoma. It focuses radiation from outside the body onto the cancer.

EBRT is much like getting an x-ray, but the radiation is stronger. A machine focuses the radiation on the area with the cancer. The procedure itself is painless, but may cause side effects. Each treatment lasts only a few minutes, but the setup time—getting you into place for treatment—usually takes longer. This therapy is usually given 5 days a

week for 4 or 5 weeks. The actual radiation treatment takes less than 30 minutes. Sometimes, a special mold of the pelvis and lower back is custom-made to be sure the person is in the exact same position for each treatment.

Brachytherapy

<u>Brachytherapy</u>³, also known as internal radiation, is another way to deliver radiation. Instead of aiming radiation beams from outside the body, a device containing radioactive materials is placed inside the body close to the tumor. People treated with this type of radiation are not radioactive after the implant is removed.

After hysterectomy, the tissues in the upper part of the vagina might need to be treated. In this situation, the radioactive material is put into the vagina. This is called **vaginal brachytherapy**.

When vaginal brachytherapy is needed, treatment is done in the radiation suite of the hospital or treatment center. About 6 to 8 weeks after the hysterectomy, the surgeon or radiation oncologist puts a special cylinder (applicator) into the vagina. The length of the cylinder (and the amount of the vagina treated) can vary, but the upper part of the vagina is always treated. Pellets of radioactive material are then put into the applicator. With this treatment, nearby structures, like the bladder and rectum, will get less radiation exposure.

There are 2 types of brachytherapy: low-dose rate (LDR) and high-dose rate (HDR).

In **LDR brachytherapy**, the radiation pellets are usually left in for 1 to 4 days at a time. The patient needs to stay very still to keep the applicator from moving during treatment, so they're usually kept in the hospital on strict bed rest. More than one treatment may be needed.

In **HDR brachytherapy**, the radiation is more intense. It's given the same way as LDR, but a higher dose of radiation is given over hours instead of days. Because the applicator is in for a shorter period of time, you can usually go home the same day. For uterine cancers, HDR brachytherapy is often given daily or weekly for a total of about 3 doses.

Side effects of radiation therapy

Short-term side effects

Short-term <u>side effects</u>⁴ of radiation therapy include:

- Feeling tired (fatigue)
- Nausea and vomiting
- · Loose stools or diarrhea
- Bladder irritation
- Skin changes
- Low blood counts

Skin changes in the treated area can look and feeling sunburned. As the radiation passes through the skin to its target, it might damage the skin cells. This can cause irritation that ranges from mild redness to permanent discoloration or skin darkening. The skin might release fluid, which can lead to infection, so care must be taken to clean and protect the area exposed to radiation.

This same kind of damage that can happen to the skin can happen inside the vagina with brachytherapy. As long as there is not a lot of bleeding, a person can continue to have sex during radiation therapy. But the outer genitals and vagina may become sore and tender to touch, and many choose to stop having sex for a while to let the area heal.

Radiation can also irritate the bladder and may cause problems urinating (peeing). Bladder irritation, called **radiation cystitis**, can cause discomfort and an urge to urinate frequently.

Almost all side effects can be treated with medicines and many go away over time after treatment ends. If you're having any side effects from radiation, discuss them with your cancer care team. There are things you can do to get relief from these symptoms or prevent them.

Long-term side effects of radiation

Radiation can also cause some side effects that can last a long time.

Radiation therapy might also cause scar tissue to form in the vagina. If the scar tissue makes the vagina shorter or more narrow it's called **vaginal stenosis**. This can make vaginal sex painful. Stretching the walls of the vagina several times a week can help prevent this problem. This can be done by having sex 3 to 4 times a week or by using a vaginal dilator (a plastic or rubber tube used much like a tampon to stretch out the vagina). Still, vaginal dryness and pain with sex can be long-term problems after radiation. Explore how radiation can impact your sex life⁵ for more information on this

topic.

Pelvic radiation can damage the ovaries, resulting in premature (early) menopause. But most women being treated for uterine sarcoma have already gone through menopause, either naturally or as a result of surgery to treat the cancer.

Radiation to the pelvis can block fluid drainage from the legs, leading to leg swelling. This is called <u>lymphedema</u>⁶. It's more common in those who had lymph nodes removed during surgery.

Pelvic radiation can also weaken bones, leading to fractures of the hips or pelvic bones. If you have had pelvic radiation, contact your doctor right away if you have pelvic pain. Such pain might be caused by a fracture, recurrent cancer, or other serious conditions, such as **hemorrhagic cystitis** (injury to the bladder with blood in the urine) or **radiation proctitis** (injury to the rectum with blood in the stool).

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy⁷.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁸.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/palliative-care.html
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html</u>
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Chemotherapy for Uterine Sarcomas

- Side effects of chemotherapy for uterine sarcoma
- More information about chemotherapy

Chemotherapy (chemo) is the use of anti-cancer drugs to treat cancer. The drugs can be taken by mouth as pills or injected by needle into a vein or muscle. These drugs enter the bloodstream and can reach almost all areas of the body, making this treatment useful for killing cancer cells in most parts of the body. This makes chemo a useful treatment for cancer that has spread outside of the uterus.

Not all women with uterine sarcoma will need chemo, but there are a few situations in which chemo might be recommended:

- After surgery (adjuvant therapy) chemo might be used to help keep the cancer from coming back later.
- Chemo might be used as the **main therapy** to treat the cancer if you are unable to have surgery.
- Sometimes chemo might be used to control uterine sarcoma that has spread to other parts of the body or come back after surgery. In this case, the goal may be to **ease symptoms** and try to keep the tumor from growing.

Chemo may not work for certain <u>types of uterine sarcoma</u>¹. And some types of uterine sarcoma have been found to respond better to certain drugs and drug combinations. The role of chemo, as well as the best chemo drugs to use are not clear. Still, a lot of <u>clinical trials</u>² are looking at this.

Some of the drugs commonly used to treat uterine sarcomas include:

Sometimes, more than one drug is used. For example, gemcitabine and docetaxel are often used together to treat leiomyosarcoma.

Side effects of chemotherapy for uterine sarcoma

These drugs kill cancer cells but can also damage some normal cells. This is what causes many <u>side effects</u>³. Side effects of chemo depend on the specific drugs, the amount taken, and the length of time you are treated.

Many side effects are short-term and go away after treatment is finished, but some can last a long time or even be permanent. It's important to tell your health care team if you have any side effects, as there are often ways to lessen them.

Some common chemo side effects include:

- Nausea and vomiting
- Loss of appetite
- Hair loss
- Mouth sores
- Feeling tired (fatigue)

Chemo can damage the blood-producing cells of the bone marrow, leading to low blood cell counts. This can cause:

- An increased chance of <u>infection</u>⁴ from a shortage of white blood cells (neutropenia)
- Problems with bleeding or bruising from a shortage of blood platelets (thrombocytopenia)
- Feeling tired or short of breath due to low red blood cell counts (anemia)

Some side effects from chemotherapy can last a long time. For example, the drug doxorubicin can damage the heart muscle over time. The chance of heart damage goes up as the total dose of the drug goes up, so doctors limit how much doxorubicin can be given.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy⁵.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁶.

Hyperlinks

1. www.cancer.org/cancer/types/uterine-sarcoma/about/what-is-uterine-sarcoma.html

- 2. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html
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- 6. www.cancer.org/cancer/managing-cancer/side-effects.html

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Hormone Therapy for Uterine Sarcomas

- Aromatase inhibitors
- Progestins
- Gonadotropin-releasing hormone agonists
- More information about hormone therapy

Hormone therapy is the use of hormones or hormone-blocking drugs to treat cancer. Part of <u>diagnosing uterine sarcoma</u>¹ includes tests that check the cancer cells to see if they have receptors (proteins) where hormones can attach. If they do have these receptors (estrogen and/or progesterone), hormone treatment might be a good option. Hormone therapy is mainly used to treat low-grade endometrial stromal sarcomas (ESS) and is rarely used for the othertypes of uterine sarcomas².

Aromatase inhibitors

After the ovaries are removed, or aren't working (after menopause), some estrogen is still made in fat tissue. This becomes the body's main source of estrogen. Drugs called **aromatase inhibitors** can stop this estrogen from being made. Examples of aromatase inhibitors include letrozole (Femara), anastrozole (Arimidex), and exemestane (Aromasin). These drugs are most often used to treat breast cancer, but they are also helpful in treating low-grade endometrial stromal sarcoma, adenosarcoma, or other sarcomas that have estrogen and/or progesterone receptors. These drugs are only useful for those whose ovaries have been removed or no longer work (like after menopause).

Side effects can include any of the symptoms of menopause, such as hot flashes and vaginal dryness, as well as joint/muscle pain. If they are taken for a long time (years), these drugs can weaken bones, sometimes leading to osteopenia or osteoporosis.

Progestins

Progestins are drugs that act like the hormone progesterone. The progestins used most often to treat estrogen-positive and/or progesterone-positive uterine sarcomas are megestrol (Megace) and medroxyprogesterone (Provera). Both of these drugs are pills you take every day.

Side effects can include increased blood sugar levels in patients with diabetes. Hot flashes, night sweats, and weight gain (from fluid retention and an increased appetite) also occur. Rarely, serious blood clots can happen in people taking progestins.

Gonadotropin-releasing hormone agonists

Gonadotropin-releasing hormone (GNRH) agonists are drugs used to lower estrogen levels in women who are premenopausal (are still having periods or have not gone through menopause). Before menopause, almost all of a woman's estrogen is made by the ovaries. These drugs keep the ovaries from making estrogen. Examples of GNRH agonists include goserelin (Zoladex) and leuprolide (Lupron). These drugs are given as a shot into a muscle every 1 to 3 months.

Side effects can include any of the symptoms of menopause, such as hot flashes and vaginal dryness. If they are taken for a long time, these drugs can weaken bones, sometimes leading to osteoporosis.

More information about hormone therapy

To learn more about how hormone therapy is used to treat cancer, see <u>Hormone Therapy</u>³.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁴.

Hyperlinks

- 1. www.cancer.org/cancer/types/uterine-sarcoma/detection-diagnosis-staging/how-diagnosed.html
- 2. www.cancer.org/cancer/types/uterine-sarcoma/about/what-is-uterine-sarcoma.html
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/hormone-therapy.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Targeted Drug Therapy for Uterine Sarcomas

- Kinase inhibitors
- TRK inhibitors
- PARP inhibitors
- More information about targeted therapy

Targeted drug therapy uses medicines that target or are directed at proteins on cancer cells that help them grow, spread, and live longer. Research has shown that some uterine sarcomas make certain proteins or have gene changes that can be targeted with specific drugs to destroy cancer cells or slow their growth. Many of these drugs can be taken as pills and their side effects are different from those of chemotherapy (sometimes less severe).

Some targeted drugs, for example, monoclonal antibodies, work in more than one way to control cancer cells and may also be considered <u>immunotherapy</u>¹ because they boost the immune system.

Kinase inhibitors

Kinases are proteins in the cell (or on its surface) that normally send signals to the rest of the cell, such as telling the cell to grow. Drugs that block certain kinases (kinase inhibitors) can help stop or slow the growth of some tumors.

Pazopanib (Votrient) is a targeted drug that might be used to treat a leiomyosarcoma that has spread or come back after treatment.

<u>Side effects</u>² include high blood pressure, diarrhea, nausea, headache, vomiting, and skin changes. More serious side effects can include bleeding in the lung or getting a hole in the bowel.

Targeted therapy is used to treat many types of cancer, but it's still new for treating uterine sarcoma.

TRK inhibitors

Some uterine sarcomas have changes in one of the NTRK genes. This gene change causes them to make abnormal TRK proteins, which can lead to abnormal cell growth and cancer.

Larotrectinib (Vitrakvi) and **entrectinib (Rozlytrek)** are drugs that target the TRK proteins. These drugs can be used to treat advanced or recurrent (cancer that has come back) uterine sarcomas with *NTRK* gene changes.

These drugs are taken as pills, once or twice a day.

Common side effects of TRK inhibitors include muscle and joint pain, cough, dizziness, fatigue, nausea, vomiting, constipation, fever, abdominal pain, and diarrhea.

PARP inhibitors

Olaparib (Lynparza), rucaparib (Rubraca), and niraparib (Zejula) are PARP inhibitors. By blocking the PARP pathway, these drugs make it very hard for tumor cells with an abnormal *BRCA* gene to repair damaged DNA, which often leads to the death of these cells. If you are not known to have a *BRCA* mutation, your doctor might test your blood or saliva to be sure you have one before starting treatment with one of these drugs.

Less than 10% of women with uterine leiomyosarcomas will have a *BRCA2* mutation. Those that do might benefit from one of these PARP inhibitors.

Olaparib (Lynparza), rucaparib (Rubraca), and niraparib (Zejula) might be used to treat advanced uterine leiomyosarcomas, typically after chemotherapy has been tried.

All of these drugs are taken daily by mouth, as pills or capsules.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>³.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁴.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy/side-effects.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Immunotherapy for Uterine Sarcomas

- Immune checkpoint inhibitors for uterine sarcomas
- More information about immunotherapy

Immunotherapy uses medicines to boost a person's own immune system to recognize and destroy cancer cells more effectively. Immunotherapy typically works on specific proteins involved in the immune system to enhance the immune response. Side effects of these drugs are different from those of chemotherapy.

Some immunotherapy drugs, for example, monoclonal antibodies, work in more than

one way to control cancer cells and may also be considered <u>targeted drug</u> <u>therapy</u>¹ because they block a specific protein on the cancer cell to keep it from growing.

Immunotherapy is used to treat some types of uterine sarcomas.

Immune checkpoint inhibitors for uterine sarcomas

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses proteins (or "checkpoints") on immune cells that need to be turned on (or off) to start an immune response. Drugs that block these checkpoint proteins, (called **immune checkpoint inhibitors**) might be used to treat some uterine sarcomas.

PD-1 inhibitor

Pembrolizumab (Keytruda) is a drug that targets PD-1 (a protein on immune system T cells that normally helps keep them from attacking other cells in the body). By blocking PD-1, these drugs boost the immune response against cancer cells. This can often shrink tumors or slow their growth.

Pembrolizumab might be an option to treat some advanced uterine sarcomas, typically after other treatments have been tried or when no other good treatment options are available, and if the cancer cells have a **high tumor mutational burden (TMB-H)**, meaning the cancer cells have many gene mutations. The tumor cells can be tested for these gene changes.

This drug is an intravenous (IV) infusion and is typically given every 3 or 6 weeks.

Possible side effects of immune checkpoint inhibitors

Side effects of these drugs can include fatigue, cough, nausea, skin rash, poor appetite, constipation, and diarrhea.

Other, more serious side effects occur less often.

Infusion reactions: Some people might have an <u>infusion reaction</u>² while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting these drugs.

Autoimmune reactions: These drugs remove one of the protections on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team quickly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>³.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁴.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Treatment for Uterine Sarcoma, by Type and Stage

- Leiomyosarcoma and undifferentiated sarcoma
- Endometrial stromal sarcoma
- Recurrent uterine sarcoma

The main treatment for early-stage uterine sarcoma is surgery to remove the uterus, sometimes along with the fallopian tubes and ovaries. In certain cases the lymph nodes might be removed and checked. Surgery might be followed by treatment with radiation, chemotherapy (chemo), or hormone therapy. Targeted drug therapy and immunotherapy might also be used in advanced cancers.

Women who can't have surgery because they have other health problems or because their cancer has spread are treated with radiation, chemo, or hormone therapy. Often some combination of these treatments is used.

Because uterine sarcoma is rare, it's has been hard to study it well. **Most experts** agree that treatment in a <u>clinical trial</u>¹ when available should be considered for any type or stage of uterine sarcoma.

Leiomyosarcoma and undifferentiated sarcoma

Stages I (1) and II (2)

Most womenhave surgery to remove the uterus (hysterectomy), as well as the fallopian tubes and ovaries (bilateral salpingo-oophorectomy). The ovaries might not be removed in women who are still having regular menstrual cycles. Pelvic and para-aortic lymph node dissection or laparoscopic lymph node sampling might be done if swollen nodes are seen on imaging tests or felt during the operation. During surgery, organs near the uterus and the thin membrane that lines the pelvic and abdominal cavities (called the peritoneum) are checked to see if the cancer has spread outside the uterus.

Some stage I cancers might not need more treatment after surgery. Observation (being watched closely after surgery) is an option. In other cases, treatment with radiation, with

or without chemo, might be needed after surgery if there's a high chance the cancer will come back. This is called **adjuvant treatment**. The goal of surgery is to take out all of the cancer, but the surgeon can only remove what can be seen. Cancer cells that are too small to be seen can be left behind. Treatments given after surgery can help kill those cancer cells so that they don't get the chance to grow. For leiomyosarcoma (LMS) of the uterus, adjuvant radiation may lower the chance of the cancer growing back in the pelvis (called **local recurrence**), but it doesn't seem to help people live longer.

Since the cancer can still come back in the lungs or other distant organs, some experts recommend giving chemo after surgery (**adjuvant chemotherapy**) for stage II cancers. Chemo is sometimes recommended for stage I LMS as well, but it's less clear that it's really helpful. Results from studies using adjuvant chemo have been promising in early-stage LMS, but so far it does not seem to help prolong life. Studies of adjuvant treatment are in progress.

Stage III (3)

Surgery is done when the surgeon feels they can remove all of the cancer. This includes removing the uterus (a hysterectomy), removing both fallopian tubes and ovaries (bilateral salpingo-oophorectomy), other organs that are involved with the tumor, and lymph node dissection or sampling. If the tumor has spread to the vagina, part (or even all) of the vagina will need to be removed as well.

After surgery, treatment with radiation or chemo might be offered to lower the chance that the cancer will come back.

People who are too sick (from other medical problems) to have surgery may be treated with chemotherapy, radiation and/or chemoradiation.

Stage IV (4)

Stage IVA cancers have spread to nearby organs and tissues, such as the bladder or rectum, and maybe to nearby lymph nodes. These cancers might be able to be completely removed with surgery, and this is usually done if possible. If the cancer cannot be removed completely, radiation might be given, either alone or followed with chemo.

Stage IVB cancers have spread outside the pelvis, most often to the lungs, liver, or bone. There's no standard treatment for these cancers. Chemo may be able to shrink the tumors for a time. Radiation therapy, followed by chemo, might also be an option.

These cancers might also be treated with targeted drug therapy or immunotherapy when other treatments don't work.

Endometrial stromal sarcoma

Stages I (1) and II (2)

Early-stage endometrial stromal sarcoma is commonly treated with surgery: hysterectomy (removal of the uterus) with or without bilateral salpingo-oophorectomy (removal of both fallopian tubes and both ovaries). Some young women who are still having regular menstrual cycles may be given the option of keeping their ovaries. Pelvic lymph nodes might be removed if they look swollen on imaging tests or feel abnormal during the operation, but this has not been shown to help women live longer.

After surgery, most women with stage I (1) cancer don't need more treatment. These women can be watched closely (observation) for any signs that the cancer has returned. Women with stage II (2) cancers might be treated with hormone therapy and sometimes radiation to the pelvis. These can lower the chances of the cancer coming back, but they have not been shown to help patients live longer. This type of uterine sarcoma does not respond well to chemo, and it's not often used at these early stages.

Women who are too sick (from other medical conditions) to have surgery may be treated with radiation and/or hormone therapy.

Stage III (3)

Surgery is done when the surgeon is able to remove all of the cancer. This includes removing the uterus (a hysterectomy), as well as removing both fallopian tubes and ovaries (bilateral salpingo-oophorectomy). Lymph nodes may be removed if they look swollen. If the tumor has spread to the vagina, part (or even all) of the vagina will need to be removed too.

Women with endometrial stromal sarcomas might get radiation, hormone therapy, or both after surgery. Chemo may be used if other treatments don't work.

Women who are too sick (from other medical conditions) to have surgery may be treated with radiation, chemo, and/or hormone therapy.

Stage IV (4)

Stage IVA cancers have spread to nearby organs and tissues, such as the bladder or rectum. These cancers may be able to be completely removed with surgery, and this is usually done if possible. If all of the cancer cannot be removed, radiation might be given, either alone or followed by chemo. Hormone therapy is also an option.

Stage IVB cancers have spread outside of the pelvis, most often to the lungs, liver, or bone. Hormone therapy can help. Chemo and radiation are also options to help ease symptoms. Targeted drug therapy and immunotherapy might also be recommended depending on certain features of the cancer.

Recurrent uterine sarcoma

If a cancer comes back after treatment, it's called **recurrent cancer**. If it comes back in the same place as it was before, it's called a **local recurrence**. For uterine sarcoma, the cancer growing back as a tumor in the pelvis would be a local recurrence. If it comes back in another part of the body, like the liver or lungs, it's called a **distant recurrence**.

If uterine sarcoma recurs, it often comes back in the first few years after treatment.

Treatment options for recurrent uterine sarcoma are the same as those for stage IV (4) cancers. If the cancer can be removed, surgery might be done. If not already given, radiation might be used to reduce the size of the tumor and relieve the symptoms of large pelvic tumors. Chemotherapy, targeted drug therapy, immunotherapy, or hormone therapy are often needed when uterine sarcoma recurs. Easing symptoms caused by cancer is called <u>palliative or supportive care</u>².

If uterine sarcoma comes back, you might want to take part in a <u>clinical trial</u>³ (scientific studies of promising treatments) testing new chemo or other treatments.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 2. www.cancer.org/cancer/managing-cancer/palliative-care.html
- 3. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>

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