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#Reference From NCCN Guidelines

Ovarian Cancer

Contents

- 4 Ovarian cancer basics
- 9 Testing for ovarian cancer
- 18 Treatment for common ovarian cancers
- 42 Treatment for less common ovarian cancers (LCOCs)
- 52 Survivorship
- 56 Making treatment decisions
- 64 Words to know
- 67 NCCN Contributors
- 68 NCCN Cancer Centers
- 70 Index

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1 Ovarian cancer basics

- 5 The ovaries
- 6 Types of ovarian cancer
- 6 Cancer care plan
- 8 Key points

Most ovarian cancers are found in the surface layer of tissue surrounding the ovaries, called the epithelium. But these cancers can also start in the fallopian tube, close to where the tube meets the ovary. This guide provides treatment recommendations for common and rare ovarian cancers.

The ovaries

The ovaries are organs in the female reproductive system. The reproductive system is the group of organs that work together for the purpose of sexual reproduction. In addition to the two ovaries, this system includes the fallopian tubes, uterus, cervix, and vagina.

Each ovary is about the size and shape of a grape. The ovaries are located in the pelvis. The pelvis is the area below the belly (abdomen) and between the hip bones. One ovary is on the left side of the uterus and the other is on the right. Each ovary is surrounded by a long, thin tube called a fallopian tube.

The ovaries make eggs needed for sexual reproduction. They also release hormones that affect breast growth, body shape, and the menstrual cycle. After an egg is pushed out by the ovary, it is caught by the fallopian tube and travels into the uterus. The uterus is where a

The reproductive system

The reproductive system is a group of organs that work together for the purpose of sexual reproduction. In addition to the ovaries, this system includes the fallopian tubes, uterus, cervix, and vagina.



NCCN Guidelines for Patients[®] Ovarian Cancer, 2023 fetus grows and develops during pregnancy. It is also called the womb. The uterus and at least one ovary and fallopian tube are needed for menstruation and pregnancy.

Types of ovarian cancer

Nine out 10 ovarian cancers are found in the outer surface of the ovaries, called the epithelium. There are more than 5 types of epithelial ovarian cancer. Some are more common than others. The most common forms of epithelial ovarian cancer are:

- High-grade serous carcinoma (HGSC)
- High-grade endometrioid carcinoma

Less common ovarian cancers

Rare types of ovarian cancer are called less common ovarian cancers (LCOCs) or less common ovarian histologies (LCOHs). Less common ovarian cancers can start in the epithelium, in tissues that support the ovaries, or in the reproductive (egg) cells of the ovary.

Less common **epithelial** ovarian cancers include:

- Low-grade serous carcinoma
- Low-grade endometrioid carcinoma
- Carcinosarcoma (also called malignant mixed Mullerian tumors)
- Clear cell carcinoma
- Mucinous carcinoma
- Borderline epithelial tumor (also called low malignant potential tumors)

Less common **non-epithelial** ovarian cancers include:

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- Malignant sex-cord stromal tumors
- Malignant germ cell tumors

How is the type determined?

As discussed later in this guide, surgery is the recommended first treatment for most ovarian cancers when possible. The tumor and other tissue removed during surgery are sent to a physician expert in testing cells to find disease, called a pathologist. The pathologist determines the type of ovarian cancer by examining the cancerous tissue.

The pathologist also determines the cancer grade. This is different than the cancer stage. Stages are categories that describe where the cancer has or has not spread from the ovary. The cancer grade is a rating of how fast the cancer is expected to grow and spread. It is based on how abnormal the cancer cells look under a microscope. High-grade cancers grow and spread more quickly than low-grade cancers.

Cancer care plan

Your treatment team

Treatment for ovarian cancer takes a team of experts. A gynecologic oncologist is a doctor who is an expert in surgery and chemotherapy for gynecologic cancers. **A gynecologic oncologist should perform the initial surgery for ovarian cancer when possible.** A medical oncologist is a doctor who is an expert in treating cancer with chemotherapy and other medicines.

You may also receive care from registered nurses, nurse practitioners, physician assistants, social workers, genetic counselors, sexual health experts, and others. Ask for the names and contact information of your care providers to be included in the treatment plan.

Cancer treatment may be improved if your primary care doctor is aware of and involved in your cancer care. They can help manage other health conditions that may be affected by your cancer treatment.

Cancer treatment

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

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

Keep in mind that your treatment plan may change. Testing may provide new information. How well the treatment is working may change the plan. Or you may change your mind about treatment. Any of these changes may require a new treatment plan.

Stress and symptom control

Anxiety and depression are common in people with cancer. At your cancer center, cancer navigators, social workers, and other experts can help. Help may include support groups, talk therapy, exercising, spending time with loved ones, or medication.

You may be unemployed or miss work during treatment. Or, you may have little or no health insurance. Talk to your treatment team about work, insurance, or money concerns. They will include information in the treatment plan to help you manage the costs of care. For more information, see the *NCCN Guidelines for Patients: Distress During Cancer Care* at <u>NCCN.org/patientguidelines</u> and on the <u>NCCN Patient Guides for Cancer</u> app.



Supportive care

Supportive care aims to relieve the symptoms of cancer or the side effects of cancer treatment. It can help relieve discomfort and improve quality of life. Supportive care may be given alone or in combination with cancer treatment.

Key points

The ovaries

- The ovaries are a pair of grape-sized organs in the pelvis.
- They make hormones and eggs for sexual reproduction.

Types of ovarian cancer

- Most ovarian cancers affect the outer surface of the ovaries, layer of tissue surrounding the ovaries, called epithelial ovarian cancer.
- High-grade serous carcinoma and highgrade endometrioid carcinoma are the most common types of ovarian tumors.
- Less common ovarian cancers can start in the epithelium, in tissues that support the ovaries, or in the reproductive (egg) cells of the ovary.

Cancer care plan

- Treating ovarian cancer takes a team of experts. Gynecologic oncologists and medical oncologists often work together to plan your treatment.
- Your cancer care may also include help with stress and symptoms, and supportive care.

2 Testing for ovarian cancer

- 10 Abdominal and pelvic exam
- 10 Imaging tests
- 13 Biopsy
- 14 Family history and genetic testing
- 15 Nutritional and digestive tract health
- 15 Blood tests
- 16 Biomarker testing
- 17 Key points

This chapter describes the testing used to learn more about suspected ovarian cancer, including whether surgery is possible.

Ovarian cancer can cause changes in the body that you can feel or notice. Unfortunately, you may not have symptoms until the tumor has grown large or has spread. Common symptoms include:

- Feeling bloated
- Heartburn and indigestion
- Pain in the pelvis or belly
- > Trouble eating or feeling full fast
- Having to urinate often or urgently
- Pain during sex

These symptoms can also be caused by hormonal changes or other common health problems. Ovarian cancer is more likely to be the cause if the symptoms:

- Began less than 1 year ago,
- > Occur more than 12 days per month, and
- > Are becoming more severe over time.

If your doctor suspects ovarian cancer based on your symptoms, you will have testing as described in this chapter. Testing helps determine the clinical (pre-treatment) stage. The clinical stage provides a "best guess" of how far the cancer has spread. It is a best guess because surgery is needed in order to know exactly how much cancer is in the body. Testing also helps determine whether surgery first is the best treatment. Having surgery first may not be possible based on the size and location of the tumor. It also may not be a good option for those who are otherwise not healthy enough to have surgery.

Abdominal and pelvic exam

Your doctor will do a physical exam of your abdomen and pelvis. For the abdominal exam, your doctor will feel different parts of your belly. This is to see if organs are of normal size, are soft or hard, or cause pain when touched. Your doctor will also feel for signs of fluid buildup (ascites) in the belly area or around the ovaries.

During the pelvic exam, your doctor will feel for abnormal changes in the size, shape, or position of your ovaries and uterus. A special widening instrument, called a speculum, will be used to view your vagina and cervix. A sample of cells may be removed for testing. This is known as a Pap test. It is used to detect cervical cancer or pre-cancer, not ovarian cancer.

An exam of the rectum and vagina together may also be done to assess if there is any tumor in the space between the rectum and vagina. This is called a rectovaginal exam.

Imaging tests

Imaging tests take pictures of the inside of your body. Doctors use imaging tests to check if there is a tumor in your ovaries. The pictures can show the tumor size, shape, and location. They can also show if the cancer has spread beyond your ovaries. Different types of imaging tests are used to look for ovarian cancer, plan treatment, and check treatment results.

Before the test, you may be asked to stop eating or drinking for a few hours. You may also need to remove metal objects from your body. The types of imaging tests used for ovarian cancer are described next.

Ultrasound

Ultrasound is often the first imaging test used to look for ovarian cancer. It uses sound waves to make pictures of areas inside of the body. Ultrasound is good at showing the size, shape, and location of the ovaries, fallopian tubes, uterus, and nearby tissues. It can also show if there is a mass in the ovary and whether the mass is solid or filled with fluid.

The 2 types of ultrasounds that may be used to look for ovarian cancer are described next. Both are done using a hand-held device called an ultrasound probe. Ultrasounds are generally painless, but you may feel some discomfort when the probe is inserted.

For a transabdominal ultrasound, a gel will be spread on your abdomen and pelvis. The gel helps to make the pictures clearer. Your doctor will place the probe on your skin and guide it back and forth in the gel.

For a transvaginal ultrasound, your doctor will insert the probe into your vagina. This may help the doctor see your ovaries more clearly.

СТ

A computed tomography (CT) scan uses x-rays to take many pictures of areas inside



Transvaginal ultrasound

waves to make pictures of the inside of the body. For a transvaginal ultrasound, a probe is inserted into the vagina. Ultrasounds are generally painless, but you may feel some discomfort when the probe is inserted.

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of the body from different angles. All of the images are combined to make one detailed picture of the body part.

CT scans of your chest, abdomen, and/or pelvis may be given along with other initial tests to look for ovarian cancer. This type of scan is good at showing if the cancer has spread outside of the ovaries. A CT scan may also show if nearby lymph nodes are bigger than normal. This can be a sign that the cancer has spread.

A substance called contrast may be used to make the pictures clearer. Before the scan you may be asked to drink a large glass of oral contrast. A contrast agent may also be injected into your vein. This is referred to as intravenous (IV) contrast. It may cause you to feel flushed or get hives. While rare, serious allergic reactions can occur. Tell your care team if you have had a bad (allergic) reaction to IV contrast in the past. A CT scanner is large and has a tunnel in the middle. During the scan, you will lie face up on a table that moves through the tunnel. The scanner will rotate an x-ray beam around you to take pictures from many angles. You may hear buzzing, clicking, or whirring sounds during this time.

MRI

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of areas inside the body. It does not use radiation. MRI is good at showing the spine and soft tissues. An MRI scan of your abdomen and pelvis may be used to look for ovarian cancer if the ultrasound was unclear. An MRI of your chest or liver may be used to look for signs of cancer spread. This test may also be used to check treatment results and to look for cancer spread to other parts of the body.

Getting an MRI scan is similar to getting a CT scan but takes longer. The full scan can take 1

CT scan

A CT scan is a more detailed kind of x-ray. It takes a lot of pictures, or images, from different angles. A computer then combines the images to make 3-D pictures.



NCCN Guidelines for Patients[®] Ovarian Cancer, 2023 hour or more. Like a CT scan, a contrast agent may be used to make the pictures clearer.

You will lie on a table that moves through a large tunnel in the scanning machine. The machine is more enclosed than a CT scan. If you have had a prior MRI scan and the enclosed feeling made you anxious, you can ask your doctor whether anti-anxiety medications would be helpful.

PET

In some cases, CT or MRI may be combined with positron emission tomography (PET). A PET scan shows how your cells are using a simple form of sugar, which can be helpful for identifying cancer. A sugar radiotracer is first put into your body with an injection into a vein. The radiotracer emits a small amount of energy that is detected by the machine that takes pictures. Active cancer cells use sugar faster than normal cells. This means that cancer cells look brighter in the pictures. PET is very good at showing small groups of cancer cells. This test may also be useful for showing if ovarian cancer has spread.

Chest x-ray

A chest x-ray can show if cancer has spread to your lungs. It may be ordered with other tests when ovarian cancer is first suspected or found. It may also be used to check treatment results. A chest x-ray is fast and painless and uses small amounts of radiation.

Diagnostic laparoscopy

If the cancer is advanced, you may have a diagnostic laparoscopy before treatment. The goal is to learn how much cancer is in the abdomen. It helps your doctors to decide whether surgery can be the first treatment, or if chemotherapy is needed first. This minimally invasive procedure involves making a tiny cut in the abdomen. A thin tube with a light and a camera (laparoscope) is used to view the lining of the abdomen and the surface of organs in the abdomen. Tissue samples are taken and tested for cancer cells in a lab.

Biopsy

To diagnose ovarian cancer, a sample of tissue must be removed from your body for testing. This is called a biopsy. Most often, the biopsy is done during initial surgery to remove the cancer.

Sometimes, however, a biopsy is done to diagnose ovarian cancer before surgery or other planned treatment. This may be the case if the cancer has spread too much to be removed by surgery initially and chemotherapy is needed first. In such cases, a fine-needle aspiration (FNA) biopsy or paracentesis may be used. FNA uses a very thin needle to remove a small sample of tissue from the tumor. For paracentesis, a long, thin needle is inserted through the skin of the belly to remove a sample of fluid.

The biopsy samples are sent to a pathologist for testing. A pathologist is a doctor who is an expert in testing cells to find disease. The pathologist views the samples with a microscope to look for cancer cells. If the cells are cancerous, the pathologist notes their appearance and other features.

Prior surgery or biopsy

The cancer may have been found during a surgery or biopsy performed by another doctor. In this case, your doctors will need to review all of the prior surgery and testing results. A pathologist will examine the tumor tissue with a microscope to make sure it is ovarian cancer. Your doctors will also want to know if any cancer was left in your body after surgery. All of this will help your current doctors plan treatment.

Family history and genetic testing

Ovarian cancer most often occurs for unknown reasons. However, about 1 in 6 ovarian cancers is caused by mutations (changes) in genes that are passed down from parent to child. This is called hereditary ovarian cancer.

Hereditary ovarian cancer is most often caused by mutations in either breast cancer gene 1 (*BRCA*1) or breast cancer gene 2 (*BRCA*2). Everyone has *BRCA*1 and *BRCA*2 genes. When working properly, they are helpful. They prevent abnormal cell growth by repairing damaged cells. But mutations in these genes increase the risk of developing ovarian, breast, and some other cancers.

Another cause of hereditary ovarian cancer is Lynch syndrome. It is also called hereditary nonpolyposis colorectal cancer (HNPCC) syndrome. Lynch syndrome is the most common cause of hereditary colon and uterine cancers but can also cause ovarian and other cancers.

Ovarian cancer associated with a *BRCA* mutation or Lynch syndrome usually starts at a younger age than non-hereditary ovarian cancer. Using your age, health history, and family history, your doctor will assess how likely you are to have hereditary ovarian cancer.

Genetic testing can tell if you have a mutation in the *BRCA* genes, or in other genes

that play a role in hereditary cancer. **It is recommended for everyone diagnosed with ovarian cancer.** If initial treatment works well, *BRCA* status (whether you have a *BRCA* mutation) plays an important role in guiding decisions about maintenance therapy. Maintenance therapy is discussed in more detail on page 33.

Genetic testing may be done through your gynecology or oncology care team, or by a genetic counselor. The testing is done on normal tissue–either blood, saliva, or a cheek swab. Those with a positive genetic test or who have a strong cancer family history should see a health expert. This is typically a genetic counselor. A genetic counselor has special training to help patients understand changes in genes that are related to disease.

Genetic testing is recommended for everyone diagnosed with ovarian cancer. It can determine if you have a mutation in the *BRCA* genes, or in other genes that play a role in hereditary cancer.



NCCN Guidelines for Patients® Ovarian Cancer, 2023 In addition to testing for germline (inherited) BRCA mutations, everyone with ovarian cancer should have the tumor tested for mutations in the BRCA and related genes. Mutations in the tumor itself are known as somatic (or simply "tumor") mutations. See the "Biomarker testing" section of this chapter for more information.

Nutritional and digestive tract health

While taking your health and family history, your doctor may also ask about your diet and eating habits. Symptoms of ovarian cancer include bloating, pain in the pelvis or abdomen, difficulty eating, and feeling full quickly.

These symptoms can lead to changes in eating habits, which can affect your overall health and nutrition level. If you are eating less in general, or not eating enough healthy foods, you may not be getting enough nutrients. This can have an impact on the success of surgery and other treatment outcomes. If you need help with keeping a healthy diet or have questions about your diet, ask your doctor for a referral to a registered dietitian or nutritionist.

Your doctor may want to evaluate your gastrointestinal (GI) tract using an imaging test. The GI tract is made of the organs that food passes through when you eat. This includes your stomach, small bowel, and large bowel (rectum and colon). An imaging tool called a scope is used to examine these organs. A scope is a long, thin tube with a light and a camera that can be guided into your body. A colonoscopy is used to examine the large bowel. This involves inserting a scope into your anus and guiding it through the rectum and colon. To examine the upper GI tract, a scope is guided down the throat into the esophagus, stomach, and small bowel. This is called an upper endoscopy.

Blood tests

The following tests are not used alone to diagnose ovarian cancer, but abnormal results may signal health problems.

A **complete blood count (CBC)** measures the number of red blood cells, white blood cells, and platelets in a sample of blood. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help to control bleeding. Your blood counts may be too low or too high because of cancer or other health problems.

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

Abnormal levels may also be caused by the spread of cancer or by other diseases. The liver is an organ that does many important jobs, such as removing toxins from your blood. **Liver function tests** measure chemicals that are made or processed by the liver. Levels that are too high or low may be a sign of liver damage or cancer spread.

Tumor markers

A tumor marker is a substance found in body tissue or fluid that may be a sign of cancer. Along with other information, tumor markers can help diagnose ovarian cancer and monitor response to treatment.

A cancer antigen-125 (CA-125) test is the most common tumor marker test for ovarian cancer.

Testing for ovarian cancer » Biomarker testing

High levels of this protein in the blood may be a sign of ovarian or other cancers. A CA-125 test alone cannot diagnose ovarian cancer. Health problems that are not cancer, such as endometriosis and diverticulitis, can raise your CA-125 level. And some ovarian cancers don't cause CA-125 to rise.

Your blood may also be tested for the following tumor markers. These may be found in higher-than-normal amounts in people with less common ovarian cancers (LCOCs).

- > Inhibin (typically inhibin A and inhibin B)
- > Beta-human chorionic gonadotropin (β -hCG)
- Alpha-fetoprotein (AFP)
- Lactate dehydrogenase (LDH)
- Carcinoembryonic antigen (CEA)
- > CA 19-9

Biomarker testing

Biomarkers are features of the tumor that can help guide your treatment. Biomarkers are often mutations (changes) in the DNA of the cancer cells. Testing for biomarkers involves analyzing a piece of tumor tissue in a lab or testing a sample of blood. The results can be used to determine whether you can join certain clinical trials.

Other names for biomarker testing include molecular testing, tumor profiling, genomic testing, tumor gene testing, next-generation sequencing, mutation testing, liquid biopsy, and precision oncology.

BRCA and HRD

A *BRCA* mutation is the most important biomarker used to plan ovarian cancer treatment. Everyone diagnosed with ovarian cancer should have the tumor tested for mutations in the *BRCA* genes, and in other similar genes important in DNA repair.

This is different than genetic testing of the blood for inherited (germline) *BRCA* mutations. Mutations in the tumor itself are known as somatic or simply "tumor" mutations.

BRCA mutations are a form of homologous recombination deficiency (HRD). This means that if you have a *BRCA* mutation, the cancer is also homologous recombination deficient or "HRD positive." However, you can also be HRD positive without a *BRCA* mutation. Other changes in the tumor's DNA can make it homologous recombination deficient. Your *BRCA* and HRD status are used to guide decisions about maintenance therapy after initial treatment.

Other biomarkers

The timing of testing for the biomarkers described next can vary. Some doctors test for these (in addition to *BRCA*) early in the treatment process. Others may only test for *BRCA* and wait to see if therapies that require other biomarkers are needed. However, testing for these biomarkers should always be performed for ovarian cancer that returns after treatment (recurrent). Testing is performed on removed tumor tissue.

- Microsatellite instability (MSI)
- Mismatch repair (MMR)
- Tumor mutational burden (TMB)
- BRAF V600E mutation
- Folate receptor alpha (FRα) expression
- > RET mutations
- NTRK gene fusion

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Key points

Biopsy

- The biopsy to diagnose ovarian cancer is usually done during initial surgery.
- If the cancer has spread too much to be removed by surgery first, a biopsy may be done before treatment.

Imaging and blood tests

- Ultrasound is often the first imaging test performed for suspected ovarian cancer.
- Other imaging tests that may be included in initial testing include CT, MRI, and PET.
- Blood tests for suspected ovarian cancer include a CBC, chemistry profile, liver function tests, and tumor marker tests.

Family history and genetic testing

- Hereditary ovarian cancer is most often caused by a mutation in the BRCA genes.
- Families with a history of Lynch syndrome may also be at risk for ovarian and other cancers.
- Everyone diagnosed with ovarian cancer should have genetic testing of the blood for germline (inherited) *BRCA* and related mutations.

Biomarker testing

- Biomarker testing looks for features of the cancer, such as mutations, that can help guide your treatment.
- Everyone diagnosed with ovarian cancer should have their tumor tested for mutations in the *BRCA* genes and others important in DNA repair.



3 Treatment for common ovarian cancers

- 19 Surgery
- 22 If surgery first is not an option
- 23 Staging
- 30 Chemotherapy after surgery
- 33 Maintenance therapy
- 35 Surveillance
- 36 Recurrence
- 39 Clinical trials
- 41 Key points

The most common types of ovarian cancer are high-grade serous carcinoma and highgrade endometrioid carcinoma. These cancers are treated with surgery and chemotherapy. When possible, surgery is the first treatment. If surgery and chemotherapy work well, maintenance therapy may be an option for more advanced cancers.

Surgery

Surgery is the recommended first treatment if you are willing and able to have it. Sometimes chemotherapy is given first. **Surgery should be performed by a gynecologic oncologist.** This is a surgeon who is an expert in cancers that start in the female reproductive organs. If you cannot have surgery first, see page 22.

The main goals of surgery are to:

- Remove all or as much of the cancer as possible, and
- > Learn how far the cancer has spread.

Hysterectomy with BSO

The most common surgery for ovarian cancer is hysterectomy and bilateral salpingooophorectomy (BSO). A hysterectomy is surgery to remove the uterus. When the cervix is removed in addition to the uterus, it is called a "total" or "complete" hysterectomy. A BSO removes both ovaries and both fallopian tubes.

Pregnancy is not possible after a hysterectomy. Fertility-sparing surgery (described below) may be an option for some very early ovarian cancers that have not spread beyond the ovaries.

If cancer has spread outside the ovaries, your surgeon will attempt to remove as much of it as possible. This is called debulking or cytoreductive surgery. The extent of the surgery depends on how far the cancer has spread. It may involve removing all or part of nearby organs. Lymph nodes that look abnormal or are larger than normal will also be removed if possible.

Fertility-sparing surgery

Pregnancy is not possible after the uterus is removed. This is difficult for those wishing to get pregnant in the future. Fertility-sparing surgery may be an option. This involves removing one or both ovaries and fallopian tubes but leaving the uterus in place. Surgery to remove one ovary and its fallopian tube is called a unilateral salpingo-oophorectomy (USO). USO is only an option if the cancer is in one ovary and the cancer is appropriate for this procedure. After a USO, you may still be able to become pregnant naturally if you haven't entered menopause.

If the cancer is in both ovaries, a BSO (without hysterectomy) may be an option. While you cannot become pregnant naturally after a BSO, pregnancy may be possible using assisted reproductive approaches. One such approach is in vitro fertilization (IVF). In IVF, eggs are fertilized with sperm in a lab to create embryos. The embryos are implanted into the uterus or frozen for future use. The eggs used for IVF may be yours (removed from your ovary before surgery) or donor eggs. Donor eggs are removed from women who have volunteered to go through hormone treatment to stimulate egg production in the ovaries.

Surgical methods

A laparotomy is the most common method for ovarian cancer surgery. A laparotomy is a long surgical cut in the abdomen. It is often an up-and-down (vertical) cut from the top of the belly button down to the pelvic bone. This lets your doctor see the tumor and other organs and tissues in your abdomen and pelvis. This method is recommended most often when surgical staging (described next) or cytoreductive surgery is planned. Less often, a minimally invasive type of surgery called laparoscopy may be used. The surgery is performed through a few small cuts in the abdomen. Laparoscopy may be used in select cases, such as when cancer is only in the ovaries. This surgery should only be done by a gynecologic oncologist experienced in this method.

Surgical staging

If it does not look like the cancer has spread, surgical staging should be performed. This involves taking samples during surgery from organs and tissues where ovarian cancer often spreads. The samples are tested for cancer cells. Your surgeon will also take samples from nearby tissues where it looks like cancer hasn't spread. This is done to check for cancer cells that have spread outside the ovaries or pelvis



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and can only be seen with a microscope. These are called microscopic metastases.

The omentum and sometimes nearby lymph nodes will be removed. The omentum is the fatty layer of tissue that covers organs in the belly (abdomen). Lymph nodes are groups of disease-fighting cells where cancer can also spread. If there is fluid buildup in the abdomen, the fluid will also be sampled. If there is not fluid buildup, your doctor may "rinse" the space inside your belly with a special liquid. This is called a peritoneal washing. Samples of the liquid will then be tested for cancer cells.

Surgical staging is the most accurate way to stage ovarian cancer. The pathologic (postsurgery) stage is based on the results of surgery and tests of tissue removed during surgery. The pathologic stage provides the most accurate picture of how far the cancer has spread. Staging is discussed on page 23.

Preparing for surgery

Your treatment team will give you instructions on how to prepare for surgery. You may be asked to stop taking some medicines for a short time. You also should not eat or drink after midnight the night before the surgery.

On the day of your surgery, you will be given medicine to put you into a deep sleep so you won't feel pain. This is called general anesthesia. Surgery may take 3 or more hours to complete. More or less time may be needed depending on how much tissue is removed.

After the surgery, expect to stay in the hospital for a few days or weeks to recover. You may feel some pain and tenderness in your belly and pelvis. It may last for a few days or weeks. You may be able to return to normal activities in a few weeks. The time it takes to fully recover varies from person to person. It also varies depending on the extent of the surgery.

Premature menopause

If you have not entered menopause, surgery that removes both ovaries 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).

If you have symptoms of surgical menopause, your doctor may suggest non-hormonal medicine or hormone replacement therapy (HRT). Discussion with a menopausal symptom team is recommended to determine whether HRT is right for you.

Other risks and side effects

With any type of surgery, there are health risks and side effects. Common side effects include pain, swelling, and scars. Common side effects of ovarian cancer surgery include leg swelling, trouble urinating, and constipation. Cancer and recent abdominal surgery are risk factors for developing blood clots, also known as deep vein thrombosis (DVT). Many patients are placed on blood thinners (either oral medications or injections) for up to 4 weeks after surgery to help prevent blood clots.

All of the side effects of ovarian cancer surgery are not listed here. Ask your treatment team for a full list of possible side effects.

If surgery first is not an option

Having surgery first may not be possible due to the size and location of the tumor. It also may not be possible if you are otherwise not healthy enough for surgery.

In this case, chemotherapy is given first to shrink the cancer. You will need a biopsy to confirm that the tumor is ovarian cancer before starting chemotherapy. At this time, preferred regimens include:

- Paclitaxel + carboplatin
- Paclitaxel + carboplatin + bevacizumab + maintenance bevacizumab

While the above regimens are preferred, there are other recommended options for chemotherapy. These regimens may change as new information becomes available.

After a few cycles of chemotherapy (2 to 3 months), your doctor will check to see how well chemotherapy worked and if surgery is an option. The goal of surgery is to remove as much of the cancer as possible, as well as the ovaries, fallopian tubes, and uterus. Surgery performed after chemotherapy is called interval cytoreductive surgery (ICS).

For stage 3 disease, hyperthermic intraperitoneal chemotherapy (HIPEC) may be used during ICS. HIPEC is a technique in which chemotherapy is warmed and then circulated in the spaces between the organs of the abdomen during surgery.

If cancer improves after several cycles of chemotherapy, surgery is usually recommended. If cancer stays the same, your doctor may recommend proceeding with surgery or continuing chemotherapy to see if there is improvement.

After surgery, more chemotherapy is usually given. Maintenance therapy may follow once your cancer is in remission.

Staging

The information gained during surgery and surgical staging is used to determine the pathologic (post-surgery) stage. The pathologic stage provides the most accurate picture of how far the cancer has spread. It is used to guide treatment after surgery.

A staging system is a standard way of describing the extent of cancer in the body. There are 2 staging systems for ovarian cancer. One was developed by the American Joint Committee on Cancer (AJCC), the other by the International Federation of Gynecology and Obstetrics (FIGO). They are very similar but the FIGO system is used most often.

In the FIGO system, the cancer stage is defined by 3 main areas of cancer growth:

- > The extent of the first (primary) tumor
- The spread of cancer to nearby lymph nodes
- > The spread of cancer to distant sites

Ovarian cancer stages are numbered from 1 to 4. Doctors write the stages as I, II, III, and IV. The stages are also divided into smaller groups, called substages. This helps to describe the extent of cancer in more detail. The FIGO stages of ovarian cancer are described on the following pages.

Ovarian cancers of the same stage tend to have a similar prognosis. A prognosis is the likely or expected course and outcome of a disease. Earlier cancer stages tend to have better outcomes. Other factors not used for cancer staging, such as your general health, are also important.

Stage 1A

Cancer is in one ovary. The outer sac (capsule) of the ovary is intact. There is no cancer on the outside surface of the ovary. No cancer cells are found in ascites or washings.



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Cancer is in both ovaries. The capsules are intact and there is no cancer on the outside surface of the ovaries. No cancer cells are found in ascites or washings.



Stage 1C

Cancer is in one or both ovaries and one or more of the following has also happened:

- Stage 1C1 The capsule of the ovary broke open during surgery. This is called surgical spill.
- Stage 1C2 The capsule of the ovary broke open before surgery, or there is cancer on the outer surface of the ovary or fallopian tube.
- Stage 1C3 Cancer cells are found in ascites or washings



Treatment for common ovarian cancers » Staging

Stage 2A

There is cancer in one or both ovaries. Cancer has grown into and/or spread implants on the uterus and/or fallopian tubes.

Stage 2B

Cancer is in one or both ovaries.

Cancer has grown into and/or spread implants on other organs or tissues in the pelvis, such as the bladder, colon, or rectum.





Stage 3A1

There is cancer in one or both ovaries. Cancer has spread to lymph nodes in the back of the abdomen (retroperitoneal lymph nodes).

- Stage 3A1 (i) Cancer in the lymph nodes is 10 mm (millimeters) or smaller.
- Stage 3A1 (ii) Cancer in the lymph nodes is larger than 10 mm.

Stage 3A2

Cancer has spread to the tissue lining the abdomen. The cancer is so small it can only be seen with a microscope. There may also be cancer in lymph nodes in the back of the abdomen.



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Stage 3B

There is visible cancer on the tissue lining the abdomen. The area of cancer is smaller than a peanut (about 2 centimeters or smaller). There may also be cancer in lymph nodes in the back of the abdomen.



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Stage 3C

There is visible cancer on the tissue lining the abdomen. The area of cancer is larger than 2 cm. There might be cancer in lymph nodes in the back of the abdomen. The cancer may have also spread to the outer surface of the liver or spleen.



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Stage 4

Cancer has spread to other parts of the body.

- Stage 4A There are cancer cells in the fluid around the lungs. This is called a malignant pleural effusion.
- Stage 4B Cancer has spread to the inside of the liver or spleen, to distant lymph nodes, or to other organs outside the abdomen.



Chemotherapy after surgery

Chemotherapy is the use of medicine(s) to kill cancer cells. It is a type of systemic therapy (therapy that goes to the whole body). When given after surgery, chemotherapy is known as primary chemotherapy.

Platinum-based chemotherapy is recommended for ovarian cancer. These medicines contain the metal platinum. Carboplatin, cisplatin, and oxaliplatin are examples. A platinum drug is often given with a different type of chemotherapy drug called a taxane to treat ovarian cancer. Paclitaxel and docetaxel are taxanes.

The regimen that is best for you depends on your age, overall health, and performance status. Performance status is a rating of how easily you can do daily tasks such as bathing or dressing.

Another factor is your risk for peripheral neuropathy. This nerve problem causes pain, tingling, and numbness, often in the hands and feet. It is a common side effect of paclitaxel. Chemotherapy is given in cycles. A cycle includes days of treatment followed by days of rest. This allows the body to recover before the next treatment. The cycles vary in length depending on which drugs are used.

Stage 1

Chemotherapy is recommended after surgery for **most** newly diagnosed stage 1 cancers. Observation may be an option for a stage 1A or 1B, grade 2 endometrioid tumor. Ask your doctor if this applies to your cancer.

Six cycles are recommended for highgrade serous tumors. Three to 6 cycles are recommended for all other stage 1 tumor types. The number of cycles you receive depends on the tumor type and other factors. Many stage 1 cancers do not need further treatment after chemotherapy.

The regimens currently recommended for stage 1 cancer are listed in **Guide 1**.

Guide 1

Stage 1 ovarian cancer – options for chemotherapy after surgery

Note: These regimens may change as new information becomes available.

Paclitaxel + carboplatin every 3 weeks (preferred)

Carboplatin + liposomal doxorubicin

Docetaxel + carboplatin

Docetaxel + oxaliplatin + bevacizumab + maintenance bevacizumab (sometimes used for stage 1B/1C)

Stages 2, 3, and 4

Chemotherapy is recommended after surgery for **all** newly diagnosed stage 2, 3, and 4 ovarian cancers. A drug called bevacizumab (Avastin) may be added to chemotherapy. This targeted therapy "starves" the tumor by stopping the growth of new blood vessels that feed it.

Six cycles of chemotherapy are given for stage 2, 3, and 4 cancers. The regimens recommended at this time are listed in **Guide 2.** Next steps for these stage cancers depends on how well chemotherapy works. If there are no signs of cancer, or if the cancer improves but isn't totally gone, maintenance therapy is often the next step. See page 33 for information on maintenance therapy.

If the cancer does not improve or gets worse, see page 36. Cancer that does not improve with treatment is called persistent. It is treated the same as recurrent ovarian cancer.

Guide 2 Stages 2, 3, and 4 – options for chemotherapy after surgery

Note: These regimens may change as new information becomes available.

Paclitaxel + carboplatin every 3 weeks (a preferred regimen)

Paclitaxel + carboplatin + bevacizumab + maintenance bevacizumab (a preferred regimen)

Paclitaxel + carboplatin (both weekly, or paclitaxel weekly and carboplatin every 3 weeks)

Carboplatin + liposomal doxorubicin

Docetaxel + carboplatin

Docetaxel + carboplatin or oxaliplatin + bevacizumab + maintenance bevacizumab

Intraperitoneal (IP)/intravenous (IV) paclitaxel + cisplatin (for some stage 2 or 3 cancers)

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How chemotherapy is given

Most of the chemotherapy regimens for ovarian cancer are given intravenously. This means the medicine is put directly into your bloodstream through a vein. You may get a port to receive chemotherapy. A port is a small, round disc that is usually placed under your skin in the upper chest. It is inserted during a minor surgery and stays in the body until treatment is complete. After treatment the port can be easily removed. Once the port is removed, the skin will heal.

Chemotherapy medicine can also be slowly injected into the abdomen. This is called intraperitoneal (IP) chemotherapy. When given this way, higher doses of the drugs are delivered directly to the cancer cells in the belly area. IP chemotherapy is given through a thin tube called a catheter. The catheter is usually connected to a port placed inside the abdomen during surgery.

Monitoring during chemotherapy

Your doctor will monitor how well the chemotherapy is working and assess for side effects. Expect to have a physical exam every 1 to 3 cycles. A pelvic eand rectovaginal exam may be done at the same time. Imaging and blood tests are ordered as needed. Testing for CA-125 or other tumor markers may be performed before each cycle of chemotherapy.

Side effects of chemotherapy

The side effects of chemotherapy depend on the specific medicine being used, the dose, and other factors. In general, side effects are caused by the death of fast-growing cells, which are found in the bowel, mouth, and blood.

Side effects

Managing side effects is a shared effort between you and your care team. It is important to speak up about bothersome side effects, such as nausea and vomiting. Ask about your options for managing or relieving the effects of treatment.

More information on nausea and vomiting is available at <u>NCCN.org/patientguidelines</u> and on the <u>NCCN Patient Guides for</u> <u>Cancer</u> app.



Common side effects include:

- > Loss of appetite
- Nausea
- Vomiting
- Mouth sores
- Hair loss
- Fatigue
- Low blood cell counts
- > Increased risk of infection
- > Bleeding or bruising easily
- Nerve damage (neuropathy)

Some side effects are more likely or more severe when certain regimens are used. Side effects also differ depending on how chemotherapy is given. IP chemotherapy tends to cause more severe side effects than IV chemotherapy. This includes infections, kidney damage, pain in the belly, and nerve damage.

Not all side effects of chemotherapy are listed here. Be sure to ask your treatment team for a full list of common and rare side effects of the drugs you receive. If a side effect bothers you, tell your treatment team.

Maintenance therapy

Maintenance therapy is the use of systemic therapy after successful initial treatment for ovarian cancer. It can reduce the risk of cancer returning or extend the time until it returns or gets worse. Maintenance therapy is an option for **stage 2, 3, and 4 cancers** that respond well or very well to surgery and platinum-based chemotherapy.

PARP inhibitors (PARPi) are a newer option for maintenance therapy after initial treatment. These oral targeted therapies work best in homologous recombination deficiency (HRD)positive cancers, including those caused by a *BRCA* mutation.

HRD-positive cancers have faulty DNA repair systems. Poly ADP-ribose polymerase (PARP) is an enzyme that helps repair DNA in cancer cells. Blocking PARP enzymes from fixing damaged cancer cells allows the cancer cells to die.



There isn't much research on maintenance therapy with a PARP inhibitor after initial treatment for stage 2 ovarian cancer. If your cancer is stage 2 and you are eligible for maintenance therapy, talk to your doctor about your options.

PARP inhibitors currently used for maintenance therapy after initial treatment of ovarian cancer include:

- Olaparib (Lynparza)
- Niraparib (Zejula)
- > Rucaparib (Rubraca)

The most common side effects of PARP inhibitors are similar to those caused by chemotherapy. They include fatigue, nausea, vomiting, and low blood cell counts. Rare but serious side effects include myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).

Myelodysplastic syndrome is a cancer in which the bone marrow does not make enough healthy blood cells. There are abnormal cells in the blood and/or bone marrow. Acute myeloid leukemia is a fast-growing disease in which too many immature white blood cells are found in the bone marrow and blood. In some cases MDS can become AML.

If chemotherapy included bevacizumab

If chemotherapy included bevacizumab **and** you have a *BRCA* mutation, maintenance therapy with both bevacizumab and olaparib (a PARP inhibitor) is recommended. Treatment with a PARP inhibitor alone is also an option, but there is less data supporting this approach.

For those with known HR deficiency (the *BRCA* status may be normal or unknown), there are 2 options for maintenance therapy after chemotherapy that included bevacizumab:

- Bevacizumab + olaparib
- Bevacizumab alone

If the HR status is normal or unknown, bevacizumab alone may be recommended.

If chemotherapy did not include bevacizumab

If you have a *BRCA* mutation and chemotherapy **did not** include bevacizumab, maintenance therapy with a PARP inhibitor alone is recommended. For some stage 2 cancers with a *BRCA* mutation, observation may be an option.

If you do not have a *BRCA* mutation (or have not had a *BRCA* test), maintenance therapy with niraparib or rucaparib may be an option, especially if the cancer is HRDpositive. Observation is also an option if there was a complete (not partial) response to chemotherapy. A complete response means there are no signs of cancer in the body.



Hypersensitivity reactions

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

- ✓ How likely is it that I will have an allergic reaction to chemotherapy?
- ✓ How will I know if I'm having an allergic reaction? What are the symptoms?
- Does the staff on hand know how to manage hypersensitivity reactions?
- Will the right medical equipment be available in case I have an allergic reaction?

How long does maintenance therapy last?

The length of maintenance therapy after initial treatment depends on the specific drug(s).

Olaparib alone can be given for up to 2 years. Olaparib + bevacizumab together can be given for up to 15 months. Niraparib alone can be given for up to 3 years. Rucaparib alone can be given for up to 2 years. Keep in mind that these recommendations can change with ongoing research.

Keep in mind that any maintenance therapy will be stopped if one of the following happens:

- The cancer grows or spreads
- The side effects become too harsh or make it unsafe to continue

Surveillance

Surveillance begins when there are no signs of cancer after treatment. It is used to find early signs that cancer has come back.

Expect to see your cancer doctor on a regular basis for physical and pelvic exams after treatment.

First 2 years: Every 2 to 4 months

Next 3 years: Every 3 to 6 months

After 5 years: Once a year

Blood and imaging tests are typically done on an as-needed basis. Your doctor may order testing if you develop symptoms or if there are other reasons to suspect relapse. If your CA-125 level (or other tumor marker) was high originally, it may be checked on a regular basis after treatment.

In addition to surveillance testing, a range of other care is important for cancer survivors. See *Part 5: Survivorship* for more information.

"I truly believe that you have to go through something life changing, to gain something life affirming."

-Ovarian cancer survivor



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Recurrence

The return of cancer after treatment is called a recurrence, or a relapse. Symptoms can be a sign of recurrence. Tell your care team if you have any of the symptoms listed below.

- > Pain or bloating in your pelvis or belly
- Unexplained weight loss
- Upset stomach
- Constipation
- Trouble eating or feeling full fast
- Fatigue
- Needing to urinate often or urgently

If recurrence is suspected, imaging tests may be ordered to confirm or rule it out.

The presence of specific biomarkers helps guide treatment for recurrent ovarian cancer. If testing for the following biomarkers has not already been done, it is recommended now:

- BRCA1 and BRCA2 mutations
- Homologous recombination deficiency (HRD) status
- Microsatellite instability (MSI)
- Mismatch repair (MMR)
- Tumor mutational burden (TMB)
- BRAF V600E mutation
- Folate receptor alpha (FRα)
- > *RET* mutations
- NTRK gene fusions

Your doctor may choose to test for even more biomarkers than those listed above.

Everyone with persistent or recurrent ovarian cancer is encouraged to consider a clinical trial for treatment.

Supportive care is an option for everyone, whether you are in active treatment or not. Supportive care can relieve the symptoms of cancer and its treatment. It aims to relieve discomfort and improve quality of life.

Rising CA-125 levels

If the level of CA-125 in your blood was high originally, it will likely be checked during surveillance. If the level is going up after treatment with surgery and chemotherapy, but there are no other signs of recurrence, treatment does not need to be started right away. It can be safe to wait until you have symptoms or other signs of recurrence. Starting treatment right away does not always lead to better outcomes. In some cases, however, your doctor may prefer not to delay treatment.

Platinum-resistant cancer

Ovarian cancer is called platinum-resistant if:

- It does not improve or worsens during platinum-based chemotherapy, or
- It returns less than 6 months after successful treatment with platinum-based chemotherapy.

Because platinum-based chemotherapy did not improve your cancer, a different type of recurrence treatment is recommended. Nonplatinum chemotherapy is usually given first. Another preferred option is bevacizumab (Avastin). For tumors with the folate receptor alpha (FR α) biomarker, the targeted therapy mirvetuximab soravtansine-gynx (Elahere) is preferred for recurrence treatment. It is a type of antibody drug conjugate (ADC).

Other options may include PARP inhibitors, endocrine therapy, targeted therapy, or immunotherapy. These are described in more detail on the next pages.

Platinum-sensitive cancer

If you enter complete remission after platinumbased chemotherapy and cancer returns more than 6 months later, the cancer is considered platinum-sensitive. This means that platinumbased chemotherapy drugs work well against the cancer.

More platinum chemotherapy

Because it worked well before, platinum chemotherapy is typically recommended for recurrent platinum-sensitive disease. This is especially true for the first recurrence. The targeted therapy bevacizumab may be added to chemotherapy. Your doctor may suggest surgery to remove all visible cancer before starting recurrence treatment. This is called secondary cytoreductive surgery.

If recurrence treatment with platinumbased chemotherapy works well or very well, maintenance therapy is an option. Bevacizumab may have been included in your recurrence chemotherapy regimen. If so, it can be continued as maintenance therapy.

A PARP inhibitor may also be an option for maintenance therapy, if you have not already been treated with one. This option is recommended for patients with a *BRCA* mutation. After successful chemotherapy for recurrent cancer, maintenance therapy with a PARP inhibitor can be continued until the cancer grows or spreads, or until the side effects become intolerable or make it unsafe to continue.

PARP inhibitor

If you've tried more than 2 lines of platinumbased therapy, a PARP inhibitor may be an option for recurrence therapy. At this time, niraparib + bevacizumab is a recommended regimen. When used after recurrence treatment, the safety of maintenance therapy with a PARP inhibitor for longer than 2 years is unknown.

Biomarker-based treatment

For tumors with specific biomarkers, targeted therapy or immunotherapy may be an option.

For **NTRK gene fusion-positive** tumors, the targeted therapies larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) are recommended options.

For tumors with the **BRAF V600E mutation**, dabrafenib (Tafinlar) and trametinib (Mekinist) together is a recommended treatment option.

For **MSI-H or dMMR** tumors, immunotherapy with pembrolizumab (Keytruda) or dostarlimabgxly (Jemperli). They are checkpoint inhibitors. Pembrolizumab is also an option for **TMB-H** cancers.

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



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Treatment for common ovarian cancers » Recurrence

Endocrine therapy

Estrogen and progesterone are hormones made by the ovaries until menopause. Hormones are sometimes offered to help with symptoms of menopause, such as hot flashes. This is known as menopausal hormone therapy. It used to be called hormonal replacement therapy (HRT). This may help some ovarian cancers grow.

In some cases, treatment can be used to block these hormones from working, or to lower hormone levels. The goal is to help slow ovarian cancer growth. This is called endocrine therapy or anti-estrogen therapy. It may be used for persistent or recurrent ovarian cancer.

- Tamoxifen is a selective estrogen receptor modulator (SERM) taken by mouth.
- Aromatase inhibitors include anastrozole, exemestane, and letrozole and are taken by mouth.
- Leuprolide acetate is a luteinizing hormone-releasing hormone (LHRH) given by injection.
- Megestrol acetate is a progestin taken by mouth.

Endocrine therapy often causes symptoms of menopause, including:

- Hot flashes
- Changes in mood
- Vaginal dryness
- Trouble sleeping
- Night sweats

Other common side effects of endocrine therapy are vaginal discharge, weight gain, swelling in the hands and feet, fatigue, and less interest in sex. Blood clots are a rare but

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Advance care planning

Talking with your doctor about your prognosis can help with treatment planning. If the cancer cannot be controlled or cured, a care plan for the end of life can be made. Benefits of advance care planning include:

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

Advance care planning starts with an honest talk between you and your doctors. Just having a general idea of your prognosis will help you decide at what point you may want to stop treatment, if at all.

serious side effect of tamoxifen. Aromatase inhibitors can weaken your bones and may also cause joint and muscle pain.

Radiation therapy to help with symptoms

Depending on the specific recurrence treatment planned, radiation therapy may also be given to help with symptoms. This is known as palliative radiation therapy.

Radiation treatment to the pelvis can cause the vagina to become shorter and narrower (vaginal stenosis). This can make it uncomfortable or even painful to have sex, or to have vaginal exams by a doctor. Vaginal dilator therapy can be used to prevent or treat vaginal stenosis. A vaginal dilator is a device used to gradually stretch or widen the vagina. You can start using a dilator as soon as 2 to 4 weeks after radiation therapy has ended. You can continue to use it for as long as you want.

Clinical trials

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

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

Phases

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

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

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Finding a clinical trial

In the United States

NCCN Cancer Centers NCCN.org/cancercenters

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

Worldwide

The U.S. National Library of Medicine (NLM) <u>clinicaltrials.gov</u>

Need help finding a clinical trial?

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

Who can enroll?

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

Informed consent

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

Start the conversation

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

Frequently asked questions

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

Will I get a placebo?

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

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Key points

Surgery and staging

- Hysterectomy with BSO is the recommended first treatment for ovarian cancer whenever possible.
- Fertility-sparing surgery may be an option for ovarian cancer that has not spread beyond the ovaries.
- Ovarian cancer is often staged during surgery to determine if it has spread. This is called surgical staging.
- Surgery to remove cancer that has spread is called cytoreductive surgery.

Chemotherapy after surgery

- Platinum-based chemotherapy is recommended after surgery for most stage 1 cancers.
- Platinum-based chemotherapy is recommended after surgery for all stage 2, 3, and 4 ovarian cancers. A targeted therapy called bevacizumab may be added.

Maintenance therapy

- Maintenance therapy is recommended for many stage 2, 3, and 4 cancers that show a complete or partial response to initial treatment.
- PARP inhibitors are often an option for maintenance therapy after initial treatment. They work best in cancers with a BRCA mutation and/or HRD-positive cancers.
- If it was included in chemotherapy, bevacizumab may be given alone or with a PARP inhibitor for maintenance therapy.

Recurrence

 If not already performed, tumor biomarker testing is recommended for everyone with recurrent ovarian cancer.

Clinical trials

 Clinical trials provide access to treatments that may, in time, be approved by the FDA.

I may not be grateful for my cancer, but I am certainly grateful for the lessons it has taught me and the wonderful people that I have met along the way"

- Ovarian cancer survivor

"

4 Treatment for less common ovarian cancers (LCOCs)

- 43 Carcinosarcoma
- 43 Clear cell carcinoma
- 44 Mucinous carcinoma
- 45 Low-grade serous carcinoma and grade 1 endometrioid carcinoma
- 45 Ovarian borderline epithelial tumors
- 47 Malignant germ cell tumors
- 50 Malignant sex cord-stromal tumors
- 51 Key points

Less common ovarian cancers (LCOCs) are often diagnosed during a surgery or other procedure. Treatment for these rare cancers is often individualized. If not already done, you may have surgery first to remove any remaining cancer or to stage the cancer.

Less common ovarian cancers can start in the epithelium, in tissues that support the ovaries, or in the reproductive (egg) cells of the ovary. Less common ovarian tumors include:

- Carcinosarcoma (also called malignant mixed Müllerian tumor)
- > Clear cell carcinoma of the ovary
- Mucinous carcinoma of the ovary
- Grade 1 endometrioid carcinoma
- Low-grade serous carcinoma
- Ovarian borderline epithelial tumors (also called low malignant potential or LMP)
- Malignant sex cord-stromal tumors
- Malignant germ cell tumors

If one is available and you are eligible, receiving treatment as part of a clinical trial is strongly recommended. If a clinical trial is not an option, treatment for LCOCs should be individualized. Whether the cancer has any biomarkers can help guide treatment for these uncommon tumors. Biomarkers are features, such as mutations.

Carcinosarcoma

Carcinosarcomas are also known as malignant mixed Müllerian tumors (MMMT). These are the most aggressive type of ovarian tumor. Fertility-sparing surgery is not an option for those with a carcinosarcoma, regardless of age or the cancer stage.

Treatment

Intravenous (IV) platinum-based chemotherapy is recommended for carcinosarcoma. A preferred regimen for all stages is paclitaxel + carboplatin, given every 3 weeks. For stage 2, 3, or 4 tumors, the targeted therapy bevacizumab may be given with chemotherapy. If so, it is often continued as maintenance therapy.

When chemotherapy is over, follow-up care will begin for stage 1 tumors. For stage 2, 3 or 4 tumors, if there is a known *BRCA* mutation, maintenance therapy may be given after chemotherapy. See page 33 for more information on maintenance therapy.

Clear cell carcinoma

Clear cell carcinomas are the most common of the less common ovarian cancers. They are considered high-grade (fast-growing) tumors. Most clear cell carcinomas do not have estrogen receptors.

Treatment

Intravenous platinum-based chemotherapy is recommended. A preferred regimen for all stages is paclitaxel + carboplatin, given every 3 weeks. For stage 2, 3, or 4 tumors, the targeted therapy bevacizumab may be given with chemotherapy. If so, it is often continued as maintenance therapy. When chemotherapy is over, follow-up care will begin for **stage 1** tumors. For **stage 2, 3, or 4** tumors, if there is a known *BRCA* mutation, maintenance therapy may be given after chemotherapy. See page 34 for more information on maintenance therapy.

Mucinous carcinoma

Mucinous tumors are often found at a younger age than more common ovarian cancers. These tumors can grow so large that they fill the abdomen and pelvis. Most people have early-stage disease at the time of diagnosis. Mucinous tumors usually respond well to treatment.

Testing for mucinous carcinoma often involves a check of the gastrointestinal (GI) tract. This can help tell the difference between true mucinous ovarian carcinoma and cancer that may have spread to the ovary from the GI tract. Blood tests measuring carcinoembryonic antigen (CEA) and CA 19-9 are recommended.

Treatment

If not already done, you may have surgery to remove any remaining cancer and to surgically stage the cancer. Fertility-sparing surgery is an option for some patients with stage 1 mucinous tumors. Either chemotherapy or observation will follow.

For stage 1A and 1B tumors, observation is recommended. Stage 1C tumors may be observed or treated with systemic therapy.

Chemotherapy is recommended for all stage 2, 3, and 4 mucinous carcinomas.

The preferred chemotherapy regimens for stage 1C and stages 2 through 4 are listed in **Guide 3.**

Guide 3 Mucinous carcinoma – preferred options for chemotherapy						
Note: These regimens may change as new information becomes available.						
Stage 1C	 5-FU + leucovorin + oxaliplatin Capecitabine + oxaliplatin Paclitaxel + carboplatin (every 3 weeks) 					
Stages 2, 3, and 4	 5-FU + leucovorin + oxaliplatin with or without bevacizumab Capecitabine + oxaliplatin with or without bevacizumab Paclitaxel + carboplatin (every 3 weeks) Paclitaxel + carboplatin + bevacizumab + maintenance bevacizumab 					

Low-grade serous carcinoma and grade 1 endometrioid carcinoma

Low-grade serous carcinoma is not the same as the more commonly diagnosed highgrade serous carcinoma. Compared to highgrade serous carcinomas, low-grade serous carcinomas tend to be diagnosed at a younger age. And while they grow more slowly, lowgrade serous tumors are often more advanced when they are found.

A little over half of low-grade serous carcinomas are linked with borderline (low malignant potential) serous tumors.

Treatment

Observation is recommended for stage 1A and 2A tumors. While observation is also an option for stage 1C tumors, these cancers are often treated with chemotherapy or hormonal therapy. Treatment with either chemotherapy or hormonal therapy is recommended for all stage 2, 3, and 4 tumors.

Options for hormone therapy include aromatase inhibitors (anastrozole, letrozole, exemestane).

For chemotherapy, paclitaxel and carboplatin (given every 3 weeks) is recommended. A targeted therapy called bevacizumab may be added to chemotherapy for stage 2, 3, or 4 tumors. If so, it may be continued as maintenance therapy.

If treatment with chemotherapy is planned, your doctor may suggest maintenance hormonal therapy afterward. Options include aromatase inhibitors, leuprolide acetate, and tamoxifen.

Ovarian borderline epithelial tumors

Ovarian borderline epithelial tumors are also called low malignant potential (LMP) tumors. These rare tumors have cancer-like features, but do not invade other tissues like most cancers do.

Borderline epithelial tumors are slow-growing and respond well to treatment. Compared to more invasive types of ovarian cancer, those diagnosed with a borderline epithelial tumor tend to be younger and often have stage 1 disease. They are also often candidates for fertility-sparing surgery.

Surgery is the main treatment for borderline epithelial tumors. Both standard surgery and fertility-sparing surgery may be options. You should be evaluated by a gynecologic oncologist for this decision.

Prior complete surgery

If the cancer was completely resected and no low-grade serous carcinoma was found, observation is recommended. If low-grade serous carcinoma was found, treatment for low-grade serous carcinoma is recommended.

Fertility-sparing surgery may be an option. If you want to keep your fertility, surgery that involves removing only the ovary with cancer and its ovarian tube, along with any remaining visible cancer. This is called a unilateral salpingo-oophorectomy (USO). For some, removing both ovaries and fallopian tubes but keeping the uterus intact may be an option.

If you do not desire fertility-sparing surgery, standard ovarian cancer surgery (total hysterectomy with bilateral salpingooophorectomy [BSO]) and removal of any remaining cancer are recommended. Removal and testing of lymph nodes during surgery is considered on a case-by-case basis.

If cancer remains after prior surgery

The following information applies to those who had incomplete prior surgery for a known borderline epithelial tumor. A surgery is considered incomplete if:

- > It did not remove all of the cancer, and/or
- The cancer was not fully staged.

If your doctor suspects that cancer remains in the body, surgery is recommended when possible. This may not be possible if you are otherwise not healthy enough, or if the cancer cannot be surgically removed.

If you would like the option of having children after treatment, fertility-sparing surgery is recommended. Any remaining cancer will also be resected.

If fertility is not desired, completion surgery (hysterectomy and removal of the opposite ovary and fallopian tube) is performed. Any remaining cancer will also be resected.

After surgery (fertility-sparing or completion), the pathology team will test the removed tissues. Sometimes the tumor type changes as a result of this testing. If the final results confirm that it is borderline, follow-up care is described next.

Follow-up

Physical exams are given every 3 to 6 months for the first 5 years after treatment. After that, they are given once per year. Your doctor may also do a pelvic exam at these visits.

If CA-125 or other tumor marker levels were high at diagnosis, they should be checked

NCCN Guidelines for Patients[®] Ovarian Cancer, 2023 at each follow-up visit. Other blood tests are performed as needed. This includes a complete blood count (CBC) and chemistry profile.

Imaging is not needed on a regular basis after treatment. Imaging may be ordered if your doctor suspects that cancer has returned.

If you had fertility-sparing surgery, you may have ultrasounds after treatment. This can help catch recurrence early. Talk to your doctor about completion surgery after you've had the baby.

Relapse

The return of cancer after treatment is called a relapse or a recurrence. In the case of a relapse, debulking surgery is often recommended when possible. This surgery aims to remove all of the cancer that the surgeon can see.

The tumor type may change as a result of surgery. Treatment based on the updated tumor type is recommended.

Malignant germ cell tumors

Germ cell tumors are a non-epithelial type of ovarian cancer. They occur mainly in young people. The average age at diagnosis is 16 to 20 years. Germ cell tumors are the most common type of ovarian tumor in this age group.

These tumors are usually diagnosed at the earliest stage. Most malignant germ cell tumors have excellent treatment outcomes. After recommended treatment, more than 8 out of 10 people survive beyond 5 years.

Types of germ cell tumors include:

- Dysgerminomas
- Immature teratomas
- Embryonal tumors
- > Endodermal sinus (yolk sac) tumors.

The following tumor markers tend to be found in higher-than-normal amounts in those with a malignant germ cell tumor:

- Alpha-fetoprotein (AFP)
- Beta-human chorionic gonadotropin (β-hCG)
- Lactate dehydrogenase (LDH)

Treatment

If you want the option of having children after treatment, fertility-sparing surgery is recommended. The cancer can be any stage. Full surgical staging is performed at the same time. Surveillance after fertility-sparing surgery involves having ultrasounds on a regular basis. Talk to your doctor about completion surgery after you've had the baby.

For those who don't desire fertility preservation, completion surgery with full surgical staging is recommended. Malignant germ cell tumors are staged with the same system used for common ovarian cancers. In children or adolescents with early-stage germ cell tumors, full surgical staging may be skipped.

After surgery, chemotherapy is recommended for most malignant germ cell tumors. This includes:

- > Any stage embryonal tumor
- Any stage endodermal sinus tumor (yolk sac tumor)
- > Stage 2, 3, or 4 dysgerminoma
- > Stage 1, grade 2 or 3 immature teratoma
- > Stage 2, 3, or 4 immature teratoma
- Any stage nongestational choriocarcinoma

Some germ cell tumors do not need chemotherapy after surgery. Observation with surveillance is recommended for:

- Stage 1 dysgerminomas, and
- > Stage 1, grade 1 immature teratomas.

For tumors that need chemotherapy, 3 to 4 cycles of the BEP regimen (bleomycin + etoposide + cisplatin) is preferred. Bleomycin can damage the lungs. Expect to have tests to check how well your lungs work before chemotherapy starts.

After chemotherapy, imaging will be ordered to see how the cancer responded. If you have a complete response to chemotherapy, expect to have follow-up checks every 2 to 4 months for 2 years. If the levels of AFP and beta-HCG were high originally, these tumor markers will also be checked with blood tests. See **Guide 4**.

Guide 4 Surveillance for malignant germ cell tumors						
	Year 1	Year 2	Year 3	Years 4 to 5	After 5 years	
Dysgerminoma						
Physical exam and tumor marker blood tests	Every 2 to 3 months	Every 3 to 4 months	Every 6 months	Every 6 months	Every year	
CT of abdomen and pelvis	Every 3 to 4 months	Every 6 months	Every year	Every year	As needed	
Non-dysgerminoma						
Physical exam and tumor marker blood tests	Every 2 months	Every 2 months	Every 4 to 6 months	Every 6 months	Every year	
Imaging	CT of chest, abdomen, and pelvis every 3 to 4 months	CT of chest, abdomen, and pelvis every 4 to 6 months	CT of abdomen and pelvis every 4 to 6 months	CT of abdomen and pelvis every 6 to 12 months	As needed	

Treatment for LCOCs » Malignant germ cell tumors

Residual or recurrent disease

Sometimes the tumor does not go away completely with treatment. This is called residual disease. Or the tumor may return after treatment. This is called recurrent disease. If the tumor can still be seen on imaging tests after surgery and chemotherapy and **tumor marker levels are normal,** your doctor may suggest surgery to remove the remaining tumor tissue. Observation with imaging is also an option.

If surgery is planned, next steps depend on the results of surgery. If all of the cancer could not be removed, your doctor may recommend 2 more cycles of platinum-based chemotherapy.

For those with confirmed cancer (either residual or recurrent) after first-line chemotherapy and abnormal tumor markers (AFP and/or bet β -hCG), options to try to cure the cancer include:

- TIP chemotherapy (paclitaxel + ifosfamide + cisplatin)
- High-dose chemotherapy with stem cell rescue

For some people, a stem cell transplant will cure the cancer. If your doctor thinks a cure is possible, you should be referred to a specialized care center for a consultation about high-dose chemotherapy and stem cell rescue. The specific high-dose chemotherapy regimens used vary between cancer centers.

If treatment with TIP or high-dose chemotherapy is not possible or desired, palliative chemotherapy is an option. The goal of care is to make you more comfortable and improve your quality of life. There are many options for palliative chemotherapy. Talk to your doctor about which may be right for you.



For newly diagnosed patients who had incomplete surgical staging, treatment options depend on:

The tumor type

- The results of imaging
- The results of tumor marker testing (AFP, beta-HCG)
- 🗸 Your age
- Whether you want to preserve your fertility

For cancers with the following biomarkers, immunotherapy with a checkpoint inhibitor may also be an option.

- Microsatellite instability-high (MSI-H)
- Mismatch repair deficient (dMMR)
- Tumor mutational burden-high (TMB-H)

Radiation therapy targeting the tumor area can help relieve symptoms caused by the cancer. Also keep in mind that receiving only supportive care without other treatment is always an option.

Malignant sex cord-stromal tumors

Malignant sex cord-stromal tumors are nonepithelial. These rare tumors include granulosa cell tumors (most common) and Sertoli-Leydig cell tumors. The prognosis (outlook) for both types is good. Most people diagnosed with a malignant granulosa cell tumor have earlystage disease, and the cancer is typically slowgrowing.

Surgery to stage the cancer is recommended for malignant sex cord-stromal tumors. Lymph node dissection (removal) is generally not included in surgical staging for these tumors.

If fertility is desired and the cancer has not spread beyond the ovary, fertility-sparing surgery with full staging is an option instead. If this is planned, talk to your doctor about having completion surgery after childbearing is finished. Completion surgery removes the uterus and the remaining ovary and fallopian tube.

Next steps of care depend on the cancer stage, as determined by surgery. Malignant sex cord stromal tumors are staged with the same system used for common ovarian cancers.

Stage 1

Observation is recommended after surgery for **low-risk** stage 1 tumors.

Medium- or high-risk stage 1 tumors may be observed or treated with platinum-based chemotherapy. The chemotherapy regimens recommended at this time are listed below.

- Paclitaxel + carboplatin (preferred)
- EP (etoposide + cisplatin)
- BEP (bleomycin + etoposide + cisplatin)

Stage 2, 3, or 4

For those with a stage 2, 3, or 4 tumor, treatment options include platinum-based chemotherapy and radiation therapy. Radiation is an option only if there is a limited amount of cancer in the body. Otherwise, chemotherapy is usually given. The options for chemotherapy are the same as those listed above for medium- and high-risk stage 1 tumors.

Surveillance

Extra-long surveillance is recommended after treatment for a granulosa cell tumor. These tumors can return decades after treatment.

Physical exams are given as needed based on the cancer stage. Exams are often given once or twice a year for early-stage and lowrisk cancers. For high-risk disease, exams are given more often (about every 4 to 6 months).

Sex cord-stromal tumors, especially granulosa cell tumors, can make a protein called inhibin. If the level of inhibin in your blood was high at the time of diagnosis, your doctor may continue to check it after treatment. If the level goes up, it could be a sign of relapse. Keep in mind that a blood test alone cannot confirm that the cancer has returned.

Testing for CA-125 and other tumor markers is individualized. If your doctor recommends it, how often the testing is needed is also based on stage. Blood tests may be ordered once or twice a year if the cancer is early-stage and low-risk. For high-risk disease, testing may be ordered every 4 to 6 months.

Imaging is not needed on a regular basis after treatment. It may be ordered if you develop cancer symptoms, if tumor marker levels are high, or if there are concerning physical exam findings.

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Relapse

A relapse (also called recurrence) is the return of cancer after being cancer-free. For those with a stage 2, 3, or 4 tumor who have a relapse, options include:

- > Enrolling in a clinical trial
- Chemotherapy
- Hormone therapy

Chemotherapy is most often used. Recommended regimens include:

- Paclitaxel + carboplatin (preferred)
- EP (etoposide + cisplatin) (if not already used)
- Paclitaxel + ifosfamide
- Docetaxel
- Paclitaxel
- Bevacizumab

Regimens other than those listed above may be helpful sometimes. If hormone therapy is planned instead of chemotherapy, options include aromatase inhibitors (anastrazole, exemestane, letrozole), leuprolide (for granulosa cell tumors), and tamoxifen.

Your doctor may suggest another surgery to remove as much of the cancer as possible. Radiation therapy targeting the tumor area can help relieve symptoms caused by the cancer. Also keep in mind that receiving only supportive care without other treatment is always an option.

Key points

- Less common ovarian cancers (LCOCs) are often diagnosed during a surgery or other procedure.
- LCOCs include: carcinosarcoma, clear cell carcinoma, mucinous carcinoma, Grade 1 endometrioid carcinoma, lowgrade serous carcinoma, borderline epithelial tumors, malignant sex cordstromal tumors, and malignant germ cell tumors.
- Treatment for these rare cancers is individualized, but often involves chemotherapy.
- If not already done, you may have surgery first to remove any remaining cancer and to stage the cancer.
- If one is available and you are eligible, receiving treatment as part of a clinical trial is strongly recommended.
- If a clinical trial is not an option, treatment for LCOCs should be individualized.

5 Survivorship

- 53 Your primary care doctor
- 53 Financial concerns
- 54 Healthy habits
- 55 More information
- 55 Key points

Survivorship begins on the day you learn you have ovarian cancer. Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the longterm side effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

For many survivors, the end of treatment signals a time of celebration but also of great anxiety. This is normal. You may need support to address issues that arise from not having regular visits with your cancer care team. In addition, your treatment plan should include a schedule of follow-up cancer tests, treatment of long-term side effects, and care of your general health.

Your primary care doctor

After finishing cancer treatment, your primary care physician (PCP) will continue to play an important role in your care. Your oncologist (cancer doctor) and PCP should work together to make sure you get the follow-up care you need. This may also involve your gynecologist.

Ask your oncologist for a written survivorship care plan that includes:

 A summary of your cancer treatment history

- 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

Financial concerns

Cancer survivors face a unique financial burden. Paying for doctor visits, tests, and treatments can become unmanageable, especially for those with little or no health insurance. You may also have costs not directly related to treatment, such as travel expenses and the cost of childcare or missed work. The term financial toxicity is used to describe the problems patients face related to the cost of medical care.

Financial toxicity can affect your quality of life and access to needed health care. If you need help paying for your cancer care, financial assistance may be available. Talk with a patient navigator, your treatment team's social worker, and your hospital's financial services department. Some of the resources listed on page 62 contain helpful information on paying for cancer care.

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Healthy habits

Monitoring for the return of 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, colorectal, and skin cancer. Your primary care doctor should tell you what cancer screening tests you should have based on your age and risk level.

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. Talk to your doctor before starting a new exercise regimen. Eat a healthy diet with lots of plant-based and high-fiber foods, including vegetables, fruits, and whole grains. Try to limit simple carbohydrates and fatty foods.

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

Quit smoking

If you are a smoker, quit! Counseling and other resources are available. Your treatment team can help.



Complementary and alternative therapies

Complementary and alternative therapies may help with side effects and improve comfort and well-being during and after cancer treatment. Some of these practices and products include:

- ✓ Acupuncture
- Dietary supplements
- Eastern medicine
- Medical marijuana
- Herbal teas and preparations
- Homeopathy
- Hypnosis
- Meditation
- 🗸 Reiki
- 🗸 Yoga
- Massage therapy

If you have questions or are curious about complementary therapies, talk to your treatment team. Many cancer centers have integrative oncology programs. Integrative oncology is an approach to cancer care that combines conventional (standard) cancer treatment with complementary and alternative therapies.

More information

For more information on cancer survivorship, the following are available at <u>NCCN.org/patientguidelines</u> and on the <u>NCCN Patient Guides for Cancer</u> app:

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



These resources address topics relevant to ovarian cancer survivors, including:

- > Anxiety, depression, and distress
- Fatigue
- Pain
- Sexual health
- Sleep problems
- Healthy lifestyles
- Immunizations
- Working, insurance, and disability concerns

Key points

- Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors.
- Survivorship care is improved if your oncologist and primary care doctor work together to get the long-term care you need.
- A survivorship care plan is helpful in transitioning your care to your primary care doctor.
- Healthy habits play a key role in helping to prevent other diseases and second cancers.
- If you have concerns about paying for your cancer care, financial help may be available.

6 Making treatment decisions

- 57 It's your choice
- 57 Questions to ask
- 62 Resources

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

NCCN Guidelines for Patients® Ovarian Cancer, 2023 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 treatment

- 1. Am I able to have surgery first? Why or why not?
- 2. How do my age, general health, and other factors affect my treatment choices?
- 3. Which type of surgery do you recommend for me? How soon do I need it?
- 4. What if I am pregnant, or planning to get pregnant in the future?
- 5. Will I need chemotherapy after surgery? For how long?
- 6. Does my cancer have any biomarkers? How does this affect my treatment?
- 7. Do you consult the NCCN Guidelines® when considering treatment options?
- 8. Are you suggesting options other than what NCCN recommends? If so, why?
- 9. Do you have a clinical trial available for me? (also see next page)
- 10. How much will treatment cost? How much will my insurance company cover?

Questions about clinical trials

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

Questions about survivorship and late effects

- 1. What happens after treatment? How likely is it that I will be cancer free?
- 2. What late effects are caused by this treatment? How will these be screened?
- 3. What are the chances the cancer will return, or that I will get another type of cancer?
- 4. Who do I see for follow-up care? How often? For how many years?
- 5. What should I do if I have trouble paying for follow-up visits and tests?
- 6. What tests will I have to monitor my health? Who is responsible for scheduling them?
- 7. I am looking for a survivor support group. What supportive services or other resources can you recommend?
- 8. What happens if I move after treatment and have to change doctors? Will you help me find a new doctor?

What is your experience?

- 1. Is ovarian cancer treatment a major part of your practice?
- 2. How many patients like me have you treated?
- 3. How many of your patients have had complications? What were the complications?
- 4. What is the experience of those on your team?
- 5. Will you be consulting with experts to discuss my care? Whom will you consult?
- 6. I would like to get a second opinion. Is there someone you recommend?

Resources

Cancer Hope Network Cancerhopenetwork.org

FORCE: Facing Our Risk of Cancer Empowered facingourrisk.org

MSI Insiders Msiinsiders.org

National Cancer Institute (NCI) cancer.gov/types

National Ovarian Cancer Coalition (NOCC) Ovarian.org

Ovarcome ovarcome.org

Ovarian Cancer Research Alliance (OCRA) ocrahope.org

Sharsheret sharsheret.org

Triage Cancer Triagecancer.org

Unite for HER uniteforher.org

U.S. National Library of Medicine Clinical Trials Database <u>clinicaltrials.gov/</u>



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

NCCN.org/patients/comments



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Words to know

abdomen

The belly area between the chest and pelvis.

ascites

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

bilateral salpingo-oophorectomy (BSO)

Surgery to remove both ovaries and both fallopian tubes.

biomarker

Unique features of a cancer or tumor that can help guide treatment.

biopsy

Removal of small amounts of tissue from the body to be tested for disease.

BRCA1 or BRCA2 genes

Genes involved in DNA repair. Mutations (changes) in either of these genes increases the risk of developing breast and ovarian cancer.

cancer antigen-125 (CA-125)

A substance that may be found in high amounts in the blood of patients with ovarian cancer.

cancer grade

A rating of how much the cancer cells look like normal cells.

cancer stage

A rating of the growth and spread of cancer in the body.

capsule

The thin layer of tissue that surrounds the ovaries.

cervix

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

chemotherapy

Drugs that kill fast-growing cells throughout the body, including normal cells and cancer cells.

clear cell carcinoma of the ovary

A less common ovarian cancer (LCOC) in which the insides of the cells look clear when viewed under a microscope.

clinical trial

Research on an investigational test or treatment to assess its safety or how well it works.

cytoreductive surgery

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

debulking surgery

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

endometrioid carcinoma of the ovary

A type of epithelial ovarian cancer. Grade 2 and 3 endometrioid tumors are common. Grade 1 endometrioid tumors are less common ovarian cancers (LCOCs).

fallopian tube

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

fertility-sparing surgery

Surgery that removes one ovary and the attached fallopian tube.

genetic counseling

A discussion with a health expert about the risk for a disease caused by changes in genes.

genetic testing

Testing of the blood or saliva for germline (inherited) mutations that cause ovarian cancer. Recommended for everyone diagnosed with ovarian cancer.

gynecologic oncologist

A surgeon who is an expert in cancers that start in the female reproductive organs. A gynecologic oncologist should perform ovarian cancer surgery.

high-grade serous carcinoma (HGSC)

The most common type of ovarian cancer. Includes grade 2 and grade 3 serous tumors.

hot flashes

A health condition of intense body heat and sweat for short periods.

hyperthermic intraperitoneal chemotherapy (HIPEC)

A cancer treatment that involves filling the abdominal cavity with warmed chemotherapy drugs.

hysterectomy

Surgery to remove the uterus.

implant

Cancer cells that broke away from the first tumor and formed new tumors on the surface of nearby organs and tissues.

intraperitoneal (IP) chemotherapy

Chemotherapy drugs given directly into the belly (abdomen) through a small tube.

laparotomy

Surgery with a long, up-and-down cut through the wall of the belly (abdomen).

less common ovarian cancers (LCOC)

Rare types of ovarian cancer, some of which are epithelial cancers. Includes carcinosarcoma, clear cell carcinoma, mucinous carcinoma, grade 1 endometrioid, low-grade serous, borderline epithelial, malignant sex-cord stromal, and malignant germ cell tumors.

low-grade serous carcinoma

A less common ovarian cancer (LCOC). Includes grade 1 serous tumors.

low malignant potential (LMP) tumor

A less common ovarian cancer (LCOC) that is usually slow-growing and does not invade other tissue. Also called a borderline epithelial tumor.

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 ovarian and other cancers. Also called hereditary non-polyposis colorectal cancer (HNPCC).

maintenance therapy

Treatment given to continue (maintain) good results of prior treatment.

medical oncologist

A doctor who is an expert in treating cancer with drugs such as chemotherapy.

menopause

The point in time when menstrual periods end.

metastasis

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

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.

mucinous carcinoma of the ovary

One of 4 types of epithelial cancer. A less common ovarian cancer (LCOC).

neuropathy

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

omentum

The layer of fatty tissue that covers organs in the belly (abdomen).

ovary

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

PARP inhibitor

A type of oral targeted therapy used for maintenance therapy in some ovarian cancers.

pathologist

A doctor who is an expert in testing cells and tissue to find disease.

peritoneal cavity

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

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.

platinum-resistant

When cancer drugs made with platinum, such as cisplatin and carboplatin, do not work well against the cancer.

platinum-sensitive

When cancer drugs made with platinum, such as cisplatin and carboplatin, work well against the cancer.

relapse

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

supportive care

Treatment given to relieve the symptoms of a disease. Also called palliative care.

surgical menopause

The onset of menopause caused by surgery. Results from a sudden drop in estrogen in the body.

surgical staging

The process of finding out how far cancer has spread by performing tests and procedures during surgery to remove the cancer.

targeted therapy

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

taxane

A type of chemotherapy drug. Often given with a platinum chemotherapy drug to treat ovarian cancer.

tumor marker

A substance found in body tissue or fluid that may be a sign of cancer.

unilateral salpingo-oophorectomy (USO)

Surgery that removes one ovary and the attached fallopian tube.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer, Version 2.2023. It was adapted, reviewed, and published with help from the following people:

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

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

City of Hope National Medical Center Duarte, California 800.826.4673 • <u>cityofhope.org</u>

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

Duke Cancer Institute Durham, North Carolina 888.275.3853 • <u>dukecancerinstitute.org</u>

Fox Chase Cancer Center Philadelphia, Pennsylvania 888.369.2427 • <u>foxchase.org</u>

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

Fred Hutchinson Cancer Center Seattle, Washington 206.667.5000 • <u>fredhutch.org</u>

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

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

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

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

Roswell Park Comprehensive Cancer Center Buffalo, New York 877.275.7724 • <u>roswellpark.org</u>

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

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

Stanford Cancer Institute Stanford, California 877.668.7535 • <u>cancer.stanford.edu</u>

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

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

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

The University of Texas MD Anderson Cancer Center Houston, Texas 844.269.5922 • <u>mdanderson.org</u>

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

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University of Colorado Cancer Center Aurora, Colorado 720.848.0300 • <u>coloradocancercenter.org</u>

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

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

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 877.936.8422 • <u>vicc.org</u>

Yale Cancer Center/Smilow Cancer Hospital New Haven, Connecticut 855.4.SMILOW • <u>valecancercenter.org</u>



We want your feedback!

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

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

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Index

Index

advance care planning 38 biomarker testing 16 **BRAF V600E** 16, 36–37 BRCA genes 14-16, 33-34, 43-44 cancer grade 6 clinical trial 36, 39-40, 43, 51 endocrine therapy 38 folate receptor alpha (FRα) 16, 36 genetic testing 14-15 homologous recombination deficiency (HRD) 16, 33–34, 36 hyperthermic intraperitoneal chemotherapy (HIPEC) 22 immunotherapy 37, 49 in vitro fertilization (IVF) 19-20 less common ovarian cancers (LCOCs) 6, 16, 43–51 microsatellite instability (MSI) 16, 36-37, 49 mismatch repair (MMR) 16, 36-37, 49 NTRK gene fusion 16, 36-37 **PARP inhibitor** 33–34, 36–37 RET mutations 16, 36 supportive care 7-8, 36, 49, 51 surgical menopause 21 tumor markers 15-16, 47-51 tumor mutational burden (TMB) 16, 36–37, 49



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