

Ovarian Cancer Epithelial Ovarian Cancer

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2019

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Ovarian Cancer



✓ Step-by-step guides to the cancer care options likely to have the best results

✓ Based on treatment guidelines used by health care providers worldwide

✓ Designed to help you discuss cancer treatment with your doctors

NCCN Guidelines for Patients[®]: Ovarian Cancer, 2019

About

National Comprehensive NCCN Cancer Network®

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These guidelines are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer (Version 1.2019, March 8, 2019).

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The National Ovarian Cancer Coalition[®] is pleased to have provided critical funding necessary to ensure the production of the NCCN Guidelines for Patients[®]: Ovarian Cancer. We believe the guidelines are an important resource that informs patients and promotes best practices for healthcare professionals, and aligns with our mission "to save lives by fighting tirelessly to prevent and cure ovarian cancer and to improve the quality of life for survivors." For support or more information about our history and groundbreaking work to empower the community, please visit www.ovarian.org or call us at 1-888-OVARIAN. www.ovarian.org

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Every hour, over 28 women get diagnosed with ovarian cancer worldwide. This deadliest gynecologic cancer has no reliable screening yet. The NCCN Guidelines for women with ovarian cancer is a strong resource, for patients as well as families and caregivers. Talking about ovarian cancer, giving this "silent" disease a voice and assisting women diagnosed with this disease are integral to our mission. We thank NCCN for providing valuable guidance and bringing resourceful information to the ovarian cancer community. <u>ovarcome.org</u>

FORCE: Facing Our Risk of Cancer Empowered

As the nation's leading organization serving the hereditary breast and ovarian cancer community, FORCE is pleased to endorse the NCCN Guidelines for Patients[®]: Ovarian Cancer. This guide provides valuable, evidence-based, expert-reviewed information on the standard of care, empowering patients to make informed decisions about their treatment. <u>facingourrisk.org</u>

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Sharsheret is proud to endorse this important resource, the NCCN Guidelines for Patients[®]: Ovarian Cancer. With this critical tool in hand, women nationwide have the knowledge they need to partner with their healthcare team to navigate the often complicated world of ovarian cancer care and make informed treatment decisions. <u>sharsheret.org</u>

Ovarian Cancer Research Alliance (OCRA)

As the largest ovarian cancer research, advocacy and patient support organization, Ovarian Cancer Research Alliance commends NCCN for providing such an important and useful resource to our community. <u>ocrahope.org</u>

Ovarian & Breast Cancer Alliance of Washington State

The NCCN Guidelines for Patients[®]: Ovarian Cancer is a comprehensive, evidence-based educational tool ensuring women have the information they need to be informed advocates for partnering in their care. The Ovarian & Breast Cancer Alliance endorses the NCCN Guidelines as a valuable resource for ovarian cancer patients and their caregivers. knowthesymptoms.org















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Ovarian Cancer

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The ovaries

Learning that you have cancer is overwhelming. This chapter provides some basic information about cancer and how it affects the ovaries.

The ovaries

The ovaries are a pair of organs that are part of the reproductive system in women. The reproductive system is the group of organs that work together for the purpose of sexual reproduction. In women, this system includes the ovaries, 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 area below the belly (abdomen) and between the hip bones. One ovary is on the left side of the uterus and one is on the right. Each ovary is connected to the uterus by a long, thin tube called a fallopian tube. **See Figure 1**.

The ovaries make eggs for sexual reproduction. They also make female hormones that affect breast growth, body shape, and the menstrual cycle. Eggs pass out of the ovary and travel through the attached fallopian tube into the uterus. The uterus is where an unborn baby grows and develops during pregnancy. It is also called the womb. The uterus and at least one ovary are needed for a woman to have a menstrual cycle and to be able to become pregnant.



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Types of ovarian cancer

Types of ovarian cancer

Epithelial ovarian cancer

The ovaries are covered in a layer of tissue called the epithelium, which is made of epithelial cells. When ovarian cancer starts in epithelial cells, it is called epithelial ovarian cancer. **Most ovarian cancers start in epithelial cells.** Because epithelial ovarian cancer is the most common type, it is often simply referred to as "ovarian cancer." **See Figure 2.**

Less common ovarian cancers

The ovaries are made of other types of cells in addition to epithelial cells. This means that there are other, less common types of ovarian cancer. **Please note that this book only addresses epithelial ovarian cancer.** For your reference, these less common types of ovarian cancer are listed below. You may hear these referred to as less common ovarian histologies (LCOH). Treatment of these ovarian cancers is beyond the scope of this book.

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

Figure 2 Epithelial ovarian cancer

Most ovarian cancers start in epithelial cells. Epithelial cells form the outer layer of tissue around the ovaries. This layer of tissue is called the epithelium. Cancer that starts in these cells is called epithelial ovarian cancer.





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Cancer cells

Cancer cells

Cancer cells act differently than normal cells in three key ways. First, cancer cells grow without control. Unlike normal cells, cancer cells make new cells that aren't needed and don't die when they should. The cancer cells build up to form a primary tumor.

Second, cancer cells can grow into (invade) other tissues. This is called invasion. Normal cells don't do this. Over time, the primary tumor can grow large and invade tissues outside the ovary. Ovarian cancer often invades the fallopian tubes and uterus.

Third, unlike normal cells, cancer cells can spread to other parts of the body. This process is called metastasis. Ovarian cancer cells can break off (shed) from the primary tumor to form new tumors on the surface of nearby organs and tissues. These are called "implants" or "seeds." Implants that grow into supporting tissues of nearby organs are called invasive implants.

Cancer cells can also spread through blood or lymph vessels. Lymph is a clear fluid that gives cells water and food. It also has white blood cells that help fight germs. It travels in small tubes (vessels) to lymph nodes. Lymph nodes are small groups of disease-fighting cells that remove germs from lymph. Lymph vessels and nodes are found all over the body. **See Figure 3**.

Figure 3 Lymph vessels and nodes

Lymph vessels and nodes are found all over the body. Lymph nodes are small groups of special disease-fighting cells. Lymph nodes are connected to each other by a network of small tubes called lymph vessels.



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Symptoms

Ovarian cancer may cause certain symptoms early, or as it grows larger. The most common symptoms of ovarian cancer include:

- Feeling bloated
- Indigestion. Many patients may be told they have indigestion or heartburn and treated for this prior to having further testing.
- > Pain in the pelvis or belly (abdomen)
- > Trouble eating or feeling full fast (early satiety)
- > Feeling the need to urinate often or urgently

These symptoms can also be caused by other common health conditions. Ovarian cancer is more likely to be the cause of these symptoms if they are:

- New (began less than 1 year ago)
- Frequent and occur more than 12 days each month

If this describes you, tell your doctor about your symptoms. Unfortunately, ovarian cancer may not cause symptoms until it has grown very large or has spread.

Other symptoms may develop if the mass is large or if fluid builds up in your abdomen. Your doctor may be able to feel a mass on pelvic or abdominal exam. The buildup of fluid is called ascites and this may cause swelling of the abdomen.

Your doctor may suspect ovarian cancer based on these signs and symptoms. But, many other health conditions could be the cause. Therefore, your doctor will give more tests and exams to confirm or rule out ovarian cancer. This is described next in the next chapter.

Review

- The ovaries are a pair of organs that make eggs for sexual reproduction. They also make hormones.
- Ovarian cancer often starts in the cells that form the outer layer of tissue around the ovaries. This is called epithelial ovarian cancer.
- Cancer cells form a tumor since they don't die as they should.
- Cancer cells can break away from the first (primary) tumor and spread to other tissues and organs in the body (metastasis).
- Some symptoms of ovarian cancer include bloating, indigestion, pain in the belly or pelvis, trouble eating, and needing to urinate often or urgently.
- Many patients may be told they have indigestion or heartburn and treated for this prior to having further testing.

2 Testing for ovarian cancer

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General health tests

This chapter describes the tests used to find, diagnose, and plan treatment for ovarian cancer. They are also used to monitor your health and check treatment results.

Your doctor may suspect ovarian cancer if you have certain symptoms. Or, ovarian cancer may have been found by a prior surgery. To confirm (diagnose) ovarian cancer and plan treatment, a number of tests are needed. Guide 1 lists the different types of tests that are used for ovarian cancer. Read the next pages to learn more about these tests, including when and why each test is recommended. Some tests are done at the initial visit, while other tests are done soon after a diagnosis is made. It is helpful to ask your doctor which tests you will have and when you can expect the results.

General health tests

Medical and family history

Your medical history includes all health events in your life and any medications you've taken. Your doctors will want to know about all of your illnesses, symptoms, and any prior tests or surgeries. It may help to make a list of old and new medications to bring to your doctor's office.

Guide 1. Tests for suspected ovarian cancer

Type of test		Recommended tests
General health tests	•	 Family and medical history Genetic counseling and testing Check nutritional status Abdominal and pelvic exam
Blood tests	•	 Complete blood count Blood chemistry profile with liver function tests Total serum protein CA-125 and other tumor markers
Imaging tests	•	 Imaging of the abdomen and pelvis using ultrasound and/or CT or MRI Imaging of the chest using x-ray or CT Gastrointestinal evaluation
Tissue tests	0	BiopsyReview of tumor tissue

General health tests

Ovarian cancer and other health conditions can run in families. Therefore, your doctors will also ask about the medical history of your blood relatives. It's important to know about diseases that run in your family. This information is called a family history.

While taking your medical and family history, your doctor may also ask you questions about your nutrition. He or she will want to know about your diet. It is important to follow a healthy diet. This is true for any cancer diagnosis. Tell your doctor or nurse about your eating habits. 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.

Genetic counseling and testing

Ovarian cancer often occurs for unknown reasons. But, about 15 out of 100 ovarian cancers are due to changes in genes that are passed down from a parent to a child. This is called hereditary ovarian cancer. Using your age, medical history, and family history, your doctor will assess how likely you are to have hereditary ovarian cancer.

NCCN experts also recommend genetic counseling for all women diagnosed with ovarian cancer. Genetic counseling is a discussion with a health expert, typically a genetic counselor, about the risk for a disease caused by changes in genes.

A genetic counselor has special training to help patients understand changes in genes that are related to disease. The genetic counselor can tell you more about how likely you are to have hereditary ovarian cancer. He or she may suggest genetic testing to look for changes in genes that increase the chances of developing ovarian cancer.

BRCA1 and BRCA2

Hereditary ovarian cancer is most often caused by changes (mutations) in the *BRCA1* and *BRCA2* genes. Families with a history of Lynch syndrome, also called hereditary nonpolyposis colorectal cancer (HNPCC), may also be at risk for ovarian and other cancers. Both *BRCA* gene mutations and Lynch syndrome put women at risk for ovarian cancer starting at an early age. When normal, these genes help prevent abnormal cell growth by repairing damaged cells. Genetic testing can tell if you have a mutation in the *BRCA* genes, or in other genes that play a role in hereditary cancer. More information on genetic mutations and treatment is provided later in this book.

Abdominal and pelvic exam

Doctors often give a physical exam along with taking a medical history. A physical exam is a review of your body for signs of disease. During this exam, your doctor will listen to your lungs, heart, and intestines to assess your general health. He or she will also look at and touch parts of your body to check for abnormal changes.

Your doctor will also do a physical exam of your belly (abdomen) and pelvis—the area between your hip bones. This is called an abdominal and pelvic exam.

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, called ascites. Ascites may be found 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 will be used to view your vagina and cervix. A sample may be taken for a Pap test at this time.

Imaging tests

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.

Getting an imaging test is often easy. 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

An ultrasound is a test that uses sound waves to take pictures of the inside of the body. It is often the first imaging test given to look for ovarian cancer. 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.

This test uses a hand-held device called an ultrasound probe. The probe sends out sound waves that bounce off organs and tissues to make echoes. The probe also picks up the echoes. A computer uses the echoes to make a picture that is shown on a screen. There are two types of ultrasounds that may be used to look for ovarian cancer: transabdominal ultrasound and transvaginal ultrasound. **See Figure 4.**

For a transabdominal ultrasound, a gel will be spread on the area of skin near your ovaries. This includes your belly (abdomen) and the area between your hip bones (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. Ultrasounds are generally painless, but you may feel some discomfort when the probe is inserted.

Computed tomography (CT)

A CT scan uses x-rays to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the x-ray pictures are combined to make one detailed picture of the body part.

A CT scan 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. But, it is not good at showing small tumors. A CT scan may also show if nearby lymph nodes are bigger than normal, which can be a sign of cancer spread.

Before the CT scan, you may be given a contrast dye to make the pictures clearer. The dye may be put in a glass of water for you to drink, injected into your vein, or both. It may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctors if you have had bad reactions in the past.

A CT scan machine is large and has a tunnel in the middle. **See Figure 5.** 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.

A computer will combine all the x-ray pictures into one detailed picture. You may not get the results for a few days since a radiologist needs to see the pictures. A radiologist is an expert in reading the pictures from imaging tests.

Figure 4 Ultrasound

An ultrasound uses sound waves to make pictures of the inside of the body. An ultrasound probe sends out the sound waves. For a transabdominal ultrasound, the probe will be placed on the skin of your belly. For a transvaginal ultrasound, it will be inserted into your vagina.



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Figure 5 CT scan machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.



Imaging tests

Magnetic resonance imaging (MRI)

An MRI scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. This type of scan is good at showing the spine and soft tissues like the brain.

An MRI scan of your abdomen and pelvis may be used to look for ovarian cancer if the ultrasound was unclear. An MRI scan of your chest may be used to look for signs of cancer spread. This test may also be used to check treatment results and to assess for cancer spread to other parts of the body.

Getting an MRI scan is similar to getting a CT scan. But, MRI scans take longer to complete. The full exam can take an hour or more. For the scan, you will need to lie on a table that moves through a large tunnel in the scanning machine. The scan may cause your body to feel a bit warm. Like a CT scan, a contrast dye may be used to make the pictures clearer. You may not get the results for a few days since a radiologist needs to see and interpret the pictures.

Positron emission tomography (PET)

A PET scan shows how your cells are using a simple form of sugar. To create pictures, a sugar radiotracer first needs to be 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. Thus, 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. Sometimes, PET is combined with CT—called a PET/CT scan.

Chest x-ray

An x-ray uses small amounts of radiation to make pictures of organs and tissues inside the body. A

tumor changes the way radiation is absorbed and will show up on the x-ray picture. A chest x-ray can be used to show if cancer has spread to your lungs. This test may be given with other initial tests when ovarian cancer is first suspected or found. It may also be given after treatment to check treatment results. A chest x-ray is painless and takes about 20 minutes to complete.

Gastrointestinal (GI) evaluation

The GI tract is made of the organs that food passes through when you eat. This includes your stomach, small intestine, large intestine, and rectum. A GI evaluation is an imaging test that is used to view your GI tract. This test may be used in certain cases to check for signs of cancer spread.

This imaging test uses a scope to see inside your GI tract. A scope is a long, thin tube that can be guided into your body, often through the mouth, anus, or a surgical cut. One end of the scope has a small light and camera lens to see inside your body. At the other end of the scope is an eyepiece that your doctor looks through to see the pictures shown by the camera.

Blood tests

Doctors test blood to look for signs of disease and to assess your general health. These tests are not used to diagnose ovarian cancer, but abnormal results may signal health problems.

СВС

A CBC (**c**omplete **b**lood **c**ount) measures the number of red blood cells, white blood cells, and platelets. Your doctor will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infections, and platelets to control bleeding. Your blood counts may be abnormal—too low or too high—because of cancer or another health problem.

Blood chemistry profile

A blood chemistry profile measures the levels of different chemicals in your blood. Chemicals in your blood come from your liver, bones, and other organs and tissues. Doctors use this test to assess the health of organs such as your liver and kidneys.

Abnormal blood chemistry levels—too high or too low—may be a sign that an organ isn't working well. Abnormal levels may also be caused by the spread of cancer or by other diseases. Your doctor will consider your health and look at the whole profile when it comes to blood test results.

Liver function tests

The liver is an organ that does many important jobs, such as remove 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. Liver function tests are often done along with a blood chemistry profile.

Tumor marker tests

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

CA-125

This is the most commonly used tumor marker test for ovarian cancer. CA-125 is a protein with sugar molecules attached to it that is made by normal cells and ovarian cancer cells. High levels of CA-125 in the blood may be a sign of ovarian cancer or another health condition.

A CA-125 test measures the amount of CA-125 in the blood. This test alone cannot diagnose ovarian cancer. But, it may be done along with other initial tests if your doctor suspects ovarian cancer. It may also be done during and after treatment to check treatment results.

Other tumor markers you may be tested for are discussed next.

Inhibin

Inhibin is a hormone produced by cells in the ovaries called granulosa cells. Testing for inhibin levels may be helpful in diagnosing some less common types of ovarian tumors, including granulosa cell tumors and mucinous epithelial tumors.

Beta-human chorionic gonadotropin (β-hCG)

 β -hCG is a hormone that may be found in higher than normal amounts in patients with ovarian and other cancers. Measuring the amount of β -hCG in women with suspected ovarian cancer may help to diagnose (confirm) cancer. It may also indicate how well cancer treatment is working.

Alpha-fetoprotein

This is a protein that is usually only detectable in the blood of pregnant women, because it is produced by the fetus. An increased level of alpha-fetoprotein in a non-pregnant woman may mean that a germ cell tumor is present.

Lactate dehydrogenase (LDH)

An increased amount of this enzyme may be a sign that an ovarian germ cell tumor is present. Measuring LDH levels can also be helpful in monitoring treatment response.

Carcinoembryonic antigen (CEA)

Most adults have a very low level of this protein in their blood. The level may be higher in people with ovarian or other cancers.

CA 19-9

This tumor marker is most often associated with pancreatic cancer, but higher than normal levels may also mean that an ovarian tumor is present.

DNA mismatch repair testing

Some people have a problem with their genes that makes them unable to fix damaged DNA (deoxyribonucleic acid). In normal cells, a process called mismatch repair (MMR) fixes errors that happen when the DNA divides and makes a copy of itself. If a cell's mismatch repair system isn't working right, errors build up and cause the DNA to become unstable. This is called microsatellite instability (MSI).

There are two kinds of laboratory tests for this genetic defect. Depending on which method is used, the result will either be MSI-H (microsatellite instability-high) or dMMR (mismatch repair deficient) if you have this genetic defect. Both results mean the same thing.

The goal of testing for this tumor marker is to find out if treatment with an immune checkpoint inhibitor may help you. If your cancer is MSI-H or dMMR, it doesn't mean that treatment with an immune checkpoint inhibitor is a good option for you. There are other factors that your doctors will weigh to find out if this treatment is right for you.

Tissue tests

Biopsy

To confirm if you have ovarian cancer, a sample of tissue must be removed from your body for testing. This is called a biopsy. Doctors test tumor tissue to check for cancer cells and to look at the features of the cancer cells. Most often, the biopsy is done during surgery to remove ovarian cancer.

For some patients a biopsy may be done before treatment. This may be done if the cancer has spread too much to be removed by initial surgery. In such cases, a fine-needle aspiration (FNA) biopsy or paracentesis may be used. An FNA biopsy 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 (abdomen) to remove a sample of fluid.

The biopsy samples will be sent to a pathologist for testing. A pathologist is a doctor who's an expert in testing cells to find disease. The pathologist will view the samples with a microscope to look for cancer cells. He or she will also assess the features of the cancer cells.

Review of tumor tissue

Sometimes ovarian cancer is confirmed by a prior surgery or biopsy performed by another doctor. In this case, your doctors will need to review all of the prior results. This includes results of the surgery, biopsy, and tests of tissue that was removed. 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 the surgery left any cancer in your body. All of this will help your current doctors plan treatment done during and after treatment to check treatment results.

Review

- Imaging tests, blood tests, and tumor marker tests are used to plan treatment for ovarian cancer.
- NCCN experts recommend genetic counseling for all women diagnosed with ovarian cancer.
 Genetic counseling may help you decide whether to be tested for hereditary ovarian cancer.
- Hereditary ovarian cancer is most often caused by mutations in the BRCA1 and BRCA2 genes.
 Families with a history of Lynch syndrome may also be at risk for ovarian and other cancers.
- High levels of CA-125 in the blood may be a sign of ovarian cancer. A blood test for CA-125 may be done if your doctor suspects ovarian cancer. It may also be done during and after treatment to check treatment results.

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Surgical staging

Cancer staging is the process of finding out how far the cancer has grown and spread in your body. The cancer stage is a rating of the extent of the cancer. Doctors use cancer staging to plan which treatments are best for you. This chapter describes the staging process and defines the stages of ovarian cancer.

Surgical staging

Cancer is often staged twice. The **clinical stage** is based on tests done before surgery. It can give your doctors an idea of how far the cancer may have spread. But, to know the true extent of ovarian cancer, surgery is needed. The **pathologic stage** is based on the results of surgery and tests of tissue removed during surgery. It is the most important stage and is used to plan treatment.

During surgery to remove the cancer, your doctor will perform a number of tests to find out exactly how far it has spread. This is called surgical staging. It is the most complete and accurate way to stage ovarian cancer.

During surgical staging, your doctor will carefully inspect tissues and organs near the tumor to see where the cancer has spread.

Some tissues will be removed so they can be tested for cancer cells. This includes removing some or all of the omentum and nearby lymph nodes.

 Surgery to remove the omentum is called an omentectomy.

What to know...

- NCCN experts recommend that surgical staging be done by a gynecologic oncologist.
- A gynecologic oncologist is a surgeon who's an expert in cancers that start in a woman's reproductive organs.

 Surgery to remove nearby lymph nodes is called a lymph node dissection.

Which surgical staging procedures you will have depends on how far your doctors think the cancer has spread.

Your doctor will also take biopsy samples from nearby tissues where it looks like the cancer hasn't spread. This is done to check for cancer cells that have spread but can only be seen with a microscope. These are called microscopic metastases. Your doctor will take samples from places where ovarian cancer often spreads. **See Figure 6** on the next page.

Surgical staging

The number of samples taken depends on how far your doctor thinks the cancer has spread. Biopsy sites may include the following:

- Nearby lymph nodes groups of diseasefighting cells
- Pelvis the area below the belly (abdomen) between the hip bones
- Abdomen the belly area between the chest and pelvis
- Diaphragm the muscles below the ribs that help a person breathe
- Omentum the layer of fatty tissue covering organs in the abdomen
- Peritoneum the tissue that lines the inside of the abdomen and pelvis and covers most organs in this space

 Ascites – abnormal fluid buildup in the abdomen

If you don't have ascites, your doctor may "wash" the space inside your belly (peritoneal cavity) with a special liquid. This is called a peritoneal washing. Samples of the liquid will then be tested for cancer cells.

Figure 6 Possible biopsy sites in the abdomen and pelvis

Surgery is used for ovarian cancer staging. Biopsy samples will be taken from the tumor as well as other organs and tissues near the ovaries. This may include the diaphragm, omentum, peritoneum, ascites, and nearby lymph nodes.



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Staging systems

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

In the FIGO system, the cancer stage is defined by three 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. The stages are also divided into smaller groups. This helps to describe the extent of cancer in more detail. The next section describes each cancer stage as defined by the FIGO staging system.

Ovarian cancer stages

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. In general, earlier cancer stages have better outcomes. Other factors not used for cancer staging, such as your general health, are also very important. The FIGO stages of ovarian cancer are described next.

Stage 1

Cancer is only in one or both ovaries. Cancer has not spread to any other organs or tissues in the body.

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.

Stage 1B

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 (ruptured) during surgery. This is called surgical spill.
- Stage 1C2 The capsule of the ovary ruptured 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.

Ovarian cancer stages

Stage 2

Cancer is in one or both ovaries and has spread to other organs or tissues within the pelvis. Cancer has not spread outside the pelvis or to any lymph nodes.

Stage 2A

Cancer has grown into and/or spread implants on the uterus, fallopian tubes, ovaries, or all of these areas.

Stage 2B

Cancer has grown into and/or spread implants on other organs or tissues in the pelvis. This may include the bladder, sigmoid colon, rectum, or the peritoneum within the pelvis. The peritoneum is the tissue that lines the inside of the abdomen and pelvis and covers most organs in this space.

Stage 3

Cancer is in one or both ovaries. It has spread outside the pelvis to tissues in the belly (abdomen). And, one or both of the following has happened: 1) cancer has spread to the tissue lining the inside of the abdomen (peritoneum); or 2) cancer may have spread to lymph nodes in the back part of the abdomen behind the peritoneum.

Stage 3A1

Cancer has spread outside the pelvis, but only to lymph nodes in the back part of the abdomen—called 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, but it is so small it can only be seen with a microscope. Cancer may have also spread to lymph nodes in the back of the abdomen.

Stage 3B

Cancer has spread to the tissue lining the abdomen and it can be seen without a microscope. The areas of cancer spread are 2 cm (centimeters) or smaller. Cancer may have also spread to lymph nodes in the back of the abdomen.

Stage 3C

Cancer has spread to the tissue lining the abdomen and it can be seen without a microscope. The areas of cancer spread are larger than 2 cm. Cancer may have spread to lymph nodes in the back of the abdomen. It may have also spread to the outer surface of the liver or spleen.

Stage 4

Cancer has spread to areas far from the pelvis and abdomen, such as the lungs, brain, or skin. It may have spread to the inside of the liver or spleen. Cancer may have also spread to lymph nodes outside the abdomen—called distant lymph nodes.

Stage 4A

There are cancer cells in the fluid around the lungs. This is called pleural effusion. Cancer has not spread anywhere else outside the abdomen.

Stage 4B

Cancer has spread to the inside of the liver or spleen, to distant lymph nodes, or to other organs outside the abdomen.

Cancer grades and cell subtypes

Ovarian cancer is also classified based on what the cancer cells look like when viewed with a microscope. A pathologist will examine the cancer cells to find out the cancer grade and cell subtype. A pathologist is a doctor who's an expert in testing cells with a microscope to identify disease. Testing cancer cells from tissue removed during surgery is the only way to find out the cancer grade and cell subtype.

Cancer grades

The cancer grade is a rating of how much the cancer cells look like normal cells. The cancer grade is a sign of how fast the cancer will likely grow and spread. Based on the features of the cancer cells, the pathologist will score the cancer as Grade 1, 2, or 3.

- Grade 1 cancer cells look similar to normal cells. This is also called low grade. These cancer cells grow slowly and are less likely to spread.
- Grade 2 cancer cells look more abnormal than Grade 1, but not as abnormal as Grade 3. These cancer cells grow at a medium speed. They are more likely to spread than Grade 1, but less likely than Grade 3.
- Grade 3 cancer cells look very different from normal cells. This is also called high grade. These cancer cells grow faster and are the most likely to spread.

Some pathologists describe the grading in only two classes: high grade or low grade. Low grade includes the Grade 1 definition above. High grade includes the Grade 2 and Grade 3 definitions.

Ovarian cancer cell subtypes

Ovarian cancer is divided (classified) into smaller groups called cell subtypes. The cell subtype is based on the features of the cancer cells. A pathologist will view the cancer cells with a microscope to find out the cell subtype. There are four main cell subtypes of epithelial ovarian cancer. Serous is the most common. The other main cell subtypes are mucinous, endometrioid, and clear cell. However, all four subtypes are often treated in the same way.

Cancer care plan

Cancer care plan

Your treatment team

Treating ovarian cancer may consist of a team of gynecologic oncologist and medical oncologists. NCCN experts recommend that a gynecologic oncologist should perform the initial surgery for ovarian cancer when possible. Your gynecologic oncologist is an expert in surgery and chemotherapy for gynecologic cancers. Sometimes, a medical oncologist who is an expert in treating cancer with chemotherapy may administer treatment.

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

Cancer treatment

There is no single treatment practice that is best for all patients. There is often more than one treatment option, including clinical trials. Clinical trials study how well a treatment works and its safety.

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

Your treatment plan may change because of new information. You may change your mind about treatment. Tests may find new results. How well the treatment is working may change. Any of these changes may require a new treatment plan.

Advance care planning

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

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

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

Another part of the planning involves hospice care. Hospice care doesn't include treatment to fight the cancer but rather to reduce symptoms caused by cancer. Hospice care may be started because you aren't interested in more cancer treatment, no other cancer treatment is available, or because you may be too sick for cancer treatment.

Hospice care allows you to have the best quality of life possible. Care is given all day, every day of the week. You can choose to have hospice care at home or at a hospice center. One study found that patients and caregivers had a better quality of life when hospice care was started early.

An advance directive describes the treatment you'd want if you weren't able to make your wishes known. It also can name a person whom you'd want to make

Review

decisions for you. It is a legal paper that your doctors have to follow. It can reveal your wishes about lifesustaining machines, such as feeding tubes. It can also include your treatment wishes if your heart or lungs were to stop working. If you already have an advance directive, it may need to be updated to be legally valid.

Review

- Cancer staging is how doctors rate and describe the extent of cancer in the body.
- The cancer stage is a rating of how much the cancer has grown and spread.
- Ovarian cancer is grouped into stages to help plan treatment.
- Ovarian cancer is staged during surgery to remove the cancer—called surgical staging.
- The cancer grade is a rating of how much the cancer cells look like normal cells. The cancer grade describes how fast or slow the cancer will likely grow and spread.
- Treating ovarian cancer takes a team of experts. Gynecologic oncologists and medical oncologists often work closely together to plan the best treatment for ovarian cancer.
- Your treatment plan should include a schedule of follow-up cancer tests, treatment of long-term side effects, and care of your general health.

"

The best advice that I could offer someone facing an illness is to stay positive no matter how much it tears you down, fight for the life you deserve, and please be proactive because no one at any age, class, or race is invincible to cancer, disease, and illness."

– Christa Ovarian cancer survivor

4 Overview of cancer treatments

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4 Overview of cancer treatments

Surgery

This chapter describes the main types of treatment for ovarian cancer. This information may help you understand the treatment options listed in the following chapters. It may also help you know what to expect during treatment. Not every woman with ovarian cancer will receive every treatment listed.

Surgery

Surgery is the first and main treatment for most ovarian cancers. NCCN experts recommend that ovarian cancer surgery should be performed by a gynecologic oncologist. A gynecologic oncologist is a surgeon who is an expert in cancers that start in a woman's reproductive organs.

There are two main goals of surgical treatment for ovarian cancer:

- > Find out how far the cancer has spread.
- Remove all or as much of the cancer from your body as possible. To do so, the tumor is removed along with other organs and tissues where cancer cells have or might have spread.

A number of procedures may be done during surgical treatment for ovarian cancer. The type and extent of surgery you will have depends on many factors. This includes the tumor size, tumor location, and how far the cancer has spread. Another key factor is whether you want the option of becoming pregnant after treatment.

Types of surgical treatment

Surgical treatment often involves removing both ovaries, both fallopian tubes, and the uterus.

- Unilateral salpingo-oophorectomy (USO) is surgery to remove only one ovary and the attached fallopian tube.
- Bilateral salpingo-oophorectomy (BSO) is surgery to remove both ovaries and both fallopian tubes.
- Total abdominal hysterectomy (TAH) is surgery to remove the uterus, including the cervix.

USO is also called "fertility-sparing surgery." This is because you will still be able to become pregnant after the surgery if you haven't yet gone through menopause. A USO is only an option if the cancer is only in one ovary.

A hysterectomy is surgery to remove the uterus. When the uterus and the cervix are removed, it is called a total hysterectomy. Most often, the uterus and cervix are removed through a surgical cut in the belly (abdomen). This is called a TAH and it is done along with a BSO. You will not be able to become pregnant after a TAH and BSO.

If cancer has spread outside the ovaries, your doctor will try to remove as much of the cancer as possible. This is called *debulking surgery* or *cytoreductive surgery*. During this surgery, your doctor will attempt to remove all of the cancer that can be seen. If the surgeon is able to remove all of the tumors that are 1 cm or larger in size, the surgery is called an optimal debulking. Removal of all disease that can be seen with the eye is called no gross residual disease. Optimal debulking is linked with better treatment outcomes, particularly if there is no gross residual disease.

Surgery

Debulking surgery may remove all or part of nearby organs where cancer has spread. **See Figure 8.** This may include removing organs such as your spleen, gallbladder, and appendix. It may also remove part of your stomach, liver, pancreas, bladder, diaphragm, and intestines. Lymph nodes that look different or are larger than normal should also be removed if possible.

Surgery methods

Most often, surgery is done using a laparotomy. 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.

Thus, a laparotomy is the most common and preferred method for ovarian cancer surgery. NCCN experts recommend that it should be used when surgical staging or debulking surgery is planned. Laparoscopy is another surgery method that may be used in some cases. Laparoscopy uses a few small cuts in the abdomen instead of one big one. Small tools are inserted through the cuts to perform the surgery. One of the tools is called a laparoscope. It is a long tube with a light and camera at the end. The camera lets your doctor see your ovaries and other tissues inside your abdomen. The other tools are used to remove tissue.

Laparoscopy may be used in select cases, such as when cancer is only in the ovaries. Rarely, it may be used when cancer has spread outside the ovaries. This surgery should only be done by a gynecologic oncologist with a lot of experience.

Preparing for surgery

Your treatment team will give you instructions on how to prepare for your surgery. You may be asked to stop taking some medicines for a short time. You also

Figure 8 Debulking surgery sites

Debulking surgery removes as much cancer as possible. The extent of the surgery depends on how far the cancer has spread. It may remove all or part of nearby organs such as your liver, spleen, stomach, gallbladder, pancreas, intestines, appendix, and bladder.



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Surgery

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 three or more hours to complete. More or less time may be needed depending on how much tissue is removed.

After the surgery, you will need 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. This 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.

Risks and side effects of surgery

With any type of surgery, there are some health risks and side effects. A side effect is an unhealthy or unpleasant condition caused by treatment. Common side effects of any surgery include pain, swelling, and scars. But, the side effects of surgery can differ between people. They also differ based on the type and extent of surgery.

Some common side effects of surgery for ovarian cancer include leg swelling, trouble urinating, and constipation. If you haven't gone through menopause, then surgery that removes both ovaries will cause menopause.

Menopause is the point in time at which you will not have another menstrual period again. When caused by surgery, the symptoms of menopause may be sudden and more severe. Symptoms of menopause include hot flashes, changes in mood, trouble sleeping, vaginal dryness, weight gain, and night sweats. All of the side effects of ovarian cancer surgery are not listed here. Ask your treatment team for a full list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

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My cancer experience has been a journey of self awareness. Along the way, I have met some inspiring women who have enriched my life. As I reach my 30th year of survivorship, I realize that hope and love sustained me through those early dark days. There is no such thing as false hope; we are all entitled to hope; hope that tomorrow will be a better day. And, of course, the love of family and friends."

– Risa

Cancer survivor

Chemotherapy

Chemotherapy

Chemotherapy (often shortened to "chemo") is the use of drugs to kill cancer cells. Chemotherapy drugs kill fast-growing cells throughout the body, including cancer cells and normal cells.

Most women with ovarian cancer receive chemotherapy after primary treatment with surgery. This is called adjuvant treatment. Your doctor may also refer to this as primary chemotherapy. In certain cases, chemotherapy may be given to shrink the cancer before surgery.

Different types of chemotherapy drugs attack cancer cells in different ways. Some kill cancer cells by damaging their DNA—molecules that contain coded instructions for making and controlling cells. Others interfere with parts of cells that are needed for making new cells.

Many types of chemotherapy drugs are used for ovarian cancer. Two of the main types used are platinum agents and taxanes. Platinum agents damage DNA in cells, which stops them from making new cells and causes them to die. Some platinum agents used for ovarian cancer are carboplatin, cisplatin, and oxaliplatin.

Taxanes block certain cell parts to stop a cell from dividing into two cells. Some taxanes used for ovarian cancer are paclitaxel, paclitaxel albumin-bound, and docetaxel.

Because chemotherapy drugs differ in how they work, more than one drug is often used. A combination regimen is the use of two or more drugs. When only one drug is used, it is called a single agent. A regimen is a treatment plan that specifies the drug(s), dose, schedule, and length of treatment.

Chemotherapy is given in cycles. A cycle includes days of treatment followed by days of rest. Giving

chemotherapy in cycles lets the body have a chance to recover before the next treatment. The cycles vary in length depending on which drugs are used. Often, the cycles are 7, 14, 21, or 28 days long. The number of treatment days per cycle and the number of cycles given also vary depending on the regimen used.

How chemotherapy is given

Intravenous (IV) chemotherapy

Most of the chemotherapy drugs used to treat ovarian cancer are liquids that are slowly injected into a vein. This is called an IV infusion.

Intraperitoneal (IP) chemotherapy

Chemotherapy can also be given as a liquid that is slowly injected into the abdomen (peritoneal cavity). This is called 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 often placed inside the abdomen during surgery. Studies have shown that patients live longer when they are able to receive some of their chemotherapy in this manner.

Hyperthermic intraperitoneal chemotherapy (HIPEC)

HIPEC is a newer technique in which a chemotherapy medicine called cisplatin is warmed and then put into the space between the organs of the abdomen during surgery. At this time, NCCN experts recommend that HIPEC be considered as one of several acceptable options for women with stage 3 epithelial ovarian cancer only.

Side effects of chemotherapy

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each treatment for ovarian cancer can cause side effects. How your body will respond can't be fully known. Some people have many side effects.

4 Overview of cancer treatments

Targeted therapy

Others have few. Some side effects can be very serious while others are just unpleasant.

The side effects of chemotherapy depend on many factors, including the drug, the dose, and the person. In general, side effects are caused by the death of fast-growing cells, which are found in the intestines, mouth, and blood. As a result, common side effects include not feeling hungry, nausea, vomiting, mouth sores, hair loss, fatigue, low blood cell counts, increased risk of infection, bleeding or bruising easily, and nerve damage (neuropathy).

Some side effects are more likely or more severe when certain combination regimens are used. The docetaxel and carboplatin regimen is more likely to increase the risk of infection. The paclitaxel and carboplatin regimen is more likely to cause neuropathy. Neuropathy is a nerve problem that causes pain, tingling, and numbness in the hands and feet. 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. There may be ways to help you feel better.

Targeted therapy

Targeted therapy is treatment with drugs that target a specific or unique feature of cancer cells. These drugs stop the action of molecules that help cancer cells grow. Targeted therapy is less likely to harm normal cells than chemotherapy. Some targeted therapy drugs that are approved to treat ovarian cancer are described next. These drugs attack cancer cells in different ways.

Bevacizumab

Bevacizumab is a type of targeted therapy called an angiogenesis inhibitor. Angiogenesis is the growth of new blood vessels. Like normal cells, cancer cells need the food and oxygen delivered in blood to live and grow. Cancer cells send out signals that cause new blood vessels to grow into the tumor to "feed" it. Bevacizumab blocks these signals so that new blood vessels will not form. As a result, the cancer cells won't receive the blood they need to live.

Olaparib, rucaparib, and niraparib

Olaparib, rucaparib, and niraparib are a type of targeted therapy known as poly (ADP-ribose) polymerase (PARP) inhibitors. PARP is a protein that helps repair damaged DNA in cells.

The *BRCA*1 and *BRCA*2 genes also help repair DNA damage in cells. But, mutations in these genes prevent them from making needed repairs. When cancer cells have mutations in the *BRCA* genes, they now must rely on PARP inhibitors to repair DNA. These drugs block the action of PARP so that it can no longer repair DNA damage in any cells. If a cell is not able to repair damaged DNA, it will die.

While all three drugs work the same, each of these agents has been approved for certain uses to treat ovarian cancer. Typically, patients need to have a *BRCA1* or *BRCA2* germline mutation or a mutation in the tumor.

Pazopanib

Pazopanib is a type of targeted therapy called a tyrosine kinase inhibitor (TKI). Tyrosine kinases are proteins in cells that are important for many cell functions. This includes sending signals in cells for cell growth, survival, and death.

Some tyrosine kinases send signals that tell cancer cells to grow and divide to make new cells. Some send signals for new blood vessels to grow into the tumor so it can survive. Pazopanib targets several tyrosine kinases and blocks the signals that help cancer grow and spread. Blocking these signals may slow cancer growth.

Immunotherapy

The immune system is your body's natural defense against infection and disease. A newer type of cancer treatment called immunotherapy increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells.

Pembrolizumab

Your immune system has important white blood cells called T cells. T cells' main job is to attack harmful things in your body, like bacteria, viruses, and cancer. They do this with the help of a protein on their surface called PD-1. Cancer cells have a different protein on their surface called PD-L1. When PD-1 and PD-L1 meet, it is called an immune checkpoint. The T cell is "told" to leave the cancer cell alone instead of attacking it.

A type of drug called an immune checkpoint inhibitor stops these two proteins from meeting. This means that the T cells will do their job and attack the cancer cells. Pembrolizumab is an example of an immune checkpoint inhibitor. Pembrolizumab isn't for everyone. You may be offered treatment with pembrolizumab if ovarian cancer came back after treatment and if your tumor tested positive for a specific tumor marker (MSI-H/dMMR).

Hormone therapy

Hormone therapy is treatment that stops the body from making certain hormones or stops the action of the hormones. Hormone therapy is not used as initial treatment for ovarian cancer. But, it may be used for ovarian cancer that has come back after other treatments.

Estrogen and progesterone are hormones that help some ovarian cancers grow. Estrogen is mostly made by the ovaries and is made in small amounts by the adrenal glands, liver, and body fat. Progesterone is also mostly made by the ovaries. Blocking these hormones from working or lowering hormone levels may help slow ovarian cancer growth.

Different types of hormone therapy drugs work in different ways. The hormone therapy drugs that may be used for ovarian cancer include:

- Tamoxifen This drug stops the effect of estrogen on cancer cell growth. It is in a class of drugs called antiestrogens.
- Anastrozole, exemestane, and letrozole These drugs lower estrogen levels in the body. They are in a class of drugs called aromatase inhibitors.
- Leuprolide acetate This drug causes the ovaries to make less estrogen and progesterone. It is in a class of drugs called luteinizing hormone-releasing hormone (LHRH) agonists.
- Megestrol acetate This drug stops the effect of estrogen on cancer cell growth. It is in a class of drugs called progestins.

Hormone therapy can cause a number of side effects. A side effect is an unhealthy or unpleasant response to treatment. The side effects may be mild or severe. Symptoms of menopause are common. Such symptoms include hot flashes, changes in
4 Overview of cancer treatments

Clinical trials

mood, vaginal dryness, trouble sleeping, and night sweats. Other common side effects of hormone therapy are vaginal discharge, weight gain, swelling in the hands and feet, fatigue, and less interest in sex. Blood clots are a rare but serious side effect of tamoxifen. Aromatase inhibitors can weaken your bones and may also cause joint and muscle pain.

All of the side effects of hormone therapy are not listed here. Ask your treatment team for a full list of common and rare side effects of the drug you receive. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

Clinical trials

A clinical trial is a type of research study that people choose to take part in as part of their cancer care. Clinical trials help doctors learn how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve cancer care. This guide provides information about many of those tests and treatments used to help people with cancer.

Clinical trials go through levels or phases of testing. These phases help move the research along to find out what works best for patients with cancer.

- Phase I looks at how much of the drug to give, its side effects, and how often to give the treatment.
- Phase II also tests for side effects and how it works on a particular cancer type.
- Phase III compares the new treatment (or new use of treatment) to what is commonly used.
- Phase IV follows late side effects and if the treatment still works after a long period.

All clinical trials have a plan and are carefully led by a medical team. Patients in a clinical trial are often alike with their cancer type and general health. You can join a clinical trial when you meet certain terms (eligibility criteria).

If you decide to join a trial, you will need to review and sign a paper called an informed consent form. This form describes the clinical trial in detail, including the risks and benefits. Even after you sign consent, you can stop taking part in a clinical trial at any time.

Some benefits of a clinical trial:

- > Access to the most current cancer care
- Close monitoring by your medical team
- > You may help other patients with cancer

Some risks of a clinical trial:

- Like any test or treatment, there may be side effects
- > New tests or treatments may not work
- > You may have to visit the hospital more often

Ask your doctor or nurse if a clinical trial may be an option for you. It is very important to keep an open mind about clinical trials and talk to your medical care team about the best option for you. There may be clinical trials available where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8, *Making treatment decisions*.

Review

- Primary treatment is the main treatment used to rid the body of cancer.
- Surgery is often used as primary treatment for ovarian cancer.
- Chemotherapy drugs kill fast-growing cells, including cancer cells and normal cells.
- Targeted therapy drugs target a specific or unique feature of cancer cells.
- Hormone therapy stops the body from making certain hormones or stops the action of the hormones.
- A clinical trial studies a test or treatment to see how safe and effective it is.

5 Treatment guide: Stage 1

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5 Treatment guide: Stage 1

First steps | Surgery

This chapter presents the treatment options recommended by NCCN experts for women with newly diagnosed stage 1 epithelial ovarian cancer. Surgery is the recommended first treatment for women who are willing and able to have it.

First steps

The **clinical (pre-surgery) stage** is based on the results of initial testing you had to diagnose ovarian cancer. This likely included some or all of the below tests. These tests are explained in more detail in the *Testing for ovarian cancer* chapter on page 11.

- An abdominal/pelvic exam
- > Imaging of your pelvis, abdomen, and chest
- Blood tests (CBC and chemistry profile with liver function test)
- > Testing for CA-125 or other tumor markers
- A GI evaluation
- Review of your family history
- Referral to a gynecologic oncologist

The results of these tests provide important information needed to plan treatment. Your doctor uses the results of these initial tests to:

- Determine the clinical (pre-surgery) 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.
- Determine whether you are a good candidate for surgery. Having surgery first may not be an option for some women based

on the size and location of the tumor. Having surgery first may also not be a good option for women who are elderly, frail, have trouble doing daily activities, or who have other serious health conditions. If your doctor decides that having surgery first isn't a good choice for you, see "If surgery first isn't an option" on page 48. Otherwise, keep reading.

Determine whether fertility-sparing surgery is an option for you. If you are a good candidate for surgery and you want the option of becoming pregnant, fertility-sparing surgery may be an option for you.

Surgery

Surgery is the recommended first treatment for all women with stage 1 ovarian cancer who are willing and able to have it. The specific type of surgery that is best for you depends in part on:

- Whether you want the option of becoming pregnant (applies to premenopausal women), and
- Whether the clinical (pre-surgery) stage is 1A, 1B, or 1C.

The most commonly used surgery for stage 1 ovarian cancer is actually two surgeries—TAH and BSO These surgeries remove both ovaries, both fallopian tubes, and the uterus. Fertility-sparing surgery may be an option for some women, and is described next.

Fertility-sparing surgery

Women who have their uterus removed are not able to become pregnant. This can be difficult to accept for some younger women diagnosed with ovarian cancer. For these women, fertility-sparing surgery may be an option. In fertility-sparing surgery, one or both ovaries and fallopian tubes are removed, but the uterus is left in place. This allows you to try to

Guide 2. Surgical options for stage 1 ovarian cancer

Pre-surgery stage	Fertility-sparing options for surgery	Fertility not desired
1A	Surgery to remove one ovary and one fallopian tube (USO)	
1B	Surgery to remove both ovaries and both fallopian tubes (BSO)	Surgery to remove both ovaries, both fallopian tubes, the uterus, and the cervix (TAH and BSO)
1C	Fertility-preserving treatment may be an option for <u>some</u> women with stage 1C disease.	

become pregnant later using assisted reproductive approaches.

If you are able and willing to have surgery, See Guide 2 for your options.

Surgical staging

Regardless of which type of surgery is performed, you should also have surgical staging. Surgical staging involves taking biopsy samples of the tumor and nearby tissues to test for cancer cells. It is done to check for cancer cells that have spread outside the ovaries or pelvis and can only be seen with a microscope. These are called microscopic metastases. During surgical staging, biopsy samples will be taken from organs and tissues where ovarian cancer often spreads. The omentum and nearby lymph nodes will also be removed.

The information gained during surgery and surgical staging is used to determine the **pathologic (post-surgery) stage**. The pathologic stage is very important because it gives a much more accurate picture of how far the cancer has spread. The pathologic (post-surgery) stage is also used to determine your treatment options after surgery.

Next steps

- Treatment options after surgery are discussed next. Many women with stage 1 ovarian cancer will need chemotherapy after surgery.
- If you haven't already had a genetic risk evaluation, NCCN experts recommend doing so before beginning chemotherapy. The tumor should also be tested for mutations in the BRCA1/2 genes.

Treatment after surgery

Many women with stage 1 ovarian cancer will need chemotherapy after surgery. The treatment options depend on several factors, including the pathologic (post-surgery) stage, the cancer grade, and the tumor type (eg, endometrioid). See Guide 3.

If chemotherapy is recommended after surgery for your cancer, you should have intravenous platinum-based chemotherapy. See Guide 4 for the platinum-based chemotherapy regimens recommended by NCCN experts.

The number of chemotherapy cycles you should have depends on the tumor type. Six cycles of chemotherapy is recommended for high-grade serous tumors. Three to six cycles of chemotherapy is recommended for all other tumor types.

The regimen that is best for you depends on a number of factors. This includes your age, overall health, and performance status—a rating of how well you are able to do daily activities. Another key factor is your risk for peripheral neuropathy—a nerve problem that causes pain, tingling, and numbness typically in the hands and feet. Neuropathy is a common side effect of paclitaxel and, to a lesser degree, carboplatin. If you have a high risk for nerve problems, then docetaxel and carboplatin may be a better option for you.

Some patients may not be able to tolerate the side effects of chemotherapy. This includes women who are older than age 70, have other health problems, or have trouble doing daily activities. For these and other patients, paclitaxel and carboplatin given once a week is an option. Giving these drugs once a week may cause fewer side effects than when they are given once every three weeks. It may be better tolerated by certain patients.

Testing during chemotherapy

During treatment, your doctor should monitor how well the chemotherapy is working and assess for side effects. The ways you may be monitored are listed below.

- A physical exam should be done every 1–3 cycles. A pelvic exam may also be done at the same time.
- CBC including measurement of platelet levels (as needed)
- > Chemistry profile (as needed)
- Testing of CA-125 or other tumor markers (as needed prior to each cycle of chemotherapy)
- Imaging tests (as needed)

Other care

Stress and symptom control

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

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

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

Guide 3. Stage 1 – Treatment options after surgery

Post-surgery stage	Cancer grade	Tumor type	Treatment options after surgery
	2	Endometrioid	Option 1: Watch-and-wait (no treatment) Option 2: Intravenous platinum-based chemotherapy
1A or 1B	3	Endometrioid	Intravenous platinum-based chemotherapy
	High-grade	Serous carcinoma	Intravenous platinum-based chemotherapy
40	2 or 3	Endometrioid	Intravenous platinum-based chemotherapy
10	High-grade	Serous carcinoma	Intravenous platinum-based chemotherapy

Guide 4. Stage 1 – Chemotherapy regimens after surgery

Medicines in regimen	How often?	How many cycles?	
Paclitaxel and carboplatin (preferred)	Once every 3 weeks		
Carboplatin and liposomal doxorubicin	Once every 4 weeks	3–6 cycles for endometrioid tumors	
Docetaxel and carboplatin	Once every 3 weeks		

Supportive care

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

Next steps

See When treatment is over on page 50 to learn about monitoring for the return of ovarian cancer and what to do if ovarian cancer comes back.

6 Treatment guide: Stages 2–4

43	First steps
43	Surgery
44	Chemotherapy
45	After chemotherapy
47	Other care
48	If surgery first isn't an option



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First steps | Surgery

This chapter presents the treatment options recommended by NCCN experts for women with newly diagnosed stage 2, 3, or 4 epithelial ovarian cancer.

for women who are elderly, frail, have trouble doing daily activities, or who have other serious health conditions. If your doctor decides that having surgery first isn't a good choice for you, see "If surgery first isn't an option" on page 48. Otherwise, keep reading.

First steps

The **clinical (pre-surgery) stage** is based on the results of initial testing you had to diagnose ovarian cancer. This likely included some or all of the below tests. These tests are explained in more detail in the *Testing for ovarian cancer* chapter.

- An abdominal/pelvic exam
- > Imaging of your pelvis, abdomen, and chest
- Blood tests (CBC and chemistry profile with liver function test)
- > Testing for CA-125 or other tumor markers
- A GI evaluation
- Review of your family history
- Referral to a gynecologic oncologist

The results of these tests provide important information needed to plan treatment. Your doctor uses the results of these initial tests to:

- > Determine the clinical (pre-surgery) 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.
- Determine whether you are a good candidate for surgery. Having surgery first may not be an option for some women based on the size and location of the tumor. Having surgery first may also not be a good option

Surgery

- In women who are willing and able to have it, surgery is the recommended first treatment for stage 2, 3, or 4 ovarian cancer. This should be decided by a gynecologic oncologist prior to any chemotherapy.
- A TAH and BSO are done at the same time and remove the ovaries, fallopian tubes, and uterus.
- Surgical staging should be done during surgery. This is to check for cancer cells that have spread outside the pelvis and can only be seen with a microscope. During surgical staging, biopsy samples will be taken from nearby organs and tissues where ovarian cancer often spreads. The omentum and nearby lymph nodes will also be removed.
- Surgery may also remove all or part of organs or tissues to which the cancer has spread. This is called debulking surgery or cytoreductive surgery. It aims to remove all visible disease in your body.

Next steps

 Treatment after surgery for stages 2–4 ovarian cancer is explained on the next pages.

Chemotherapy

Chemotherapy

After surgery, platinum-based chemotherapy is recommended for all newly diagnosed women with stage 2, 3, or 4 ovarian cancer. See Guide 5 for the specific regimens recommended by NCCN experts.

Most of the chemotherapy regimens are given intravenously, meaning the medicine is put directly into your bloodstream through a vein. One of the regimens (paclitaxel and cisplatin) also uses intraperitoneal chemotherapy, in which medicine is put directly in the abdomen. This regimen has "(IP/IV)" after the name in Guide 5. It is important to discuss the differences between IV and IP chemotherapy with your doctor.

Testing during chemotherapy

During treatment, your doctor should monitor how well the chemotherapy is working and assess for side effects. The ways you may be monitored are listed below.

- A physical exam should be done every 1–3 cycles. A pelvic exam may also be done at the same time.
- CBC including measurement of platelet levels (as needed)
- > Chemistry profile (as needed)
- Testing of CA-125 or other tumor markers (as needed prior to each cycle of chemotherapy)
- Imaging tests (as needed)

Completion surgery

Depending on how well chemotherapy works, some women may have another surgery to remove any remaining ovarian cancer. This is called completion surgery. NCCN experts recommend that completion surgery be done after 3 cycles of chemotherapy. However, surgery may be performed after 4–6 cycles based on the clinical judgment of the gynecologic oncologist.

Guide 5. Stages 2, 3, and 4 – Chemotherapy after surgery

Medicines included in regimen	How often and for how long?
Paclitaxel and cisplatin (IP/IV)	Once every 3 weeks for 6 cycles
Paclitaxel and carboplatin	Option 1: Once every 3 weeks for 6 cycles Option 2: Once a week for 18 weeks (a lower dose given more often)
Docetaxel and carboplatin	Once every 3 weeks for 6 cycles
Carboplatin and liposomal doxorubicin	Once every 4 weeks for 6 cycles
Paclitaxel, carboplatin, and bevacizumab	Option 1: All three given once every 3 weeks for 5–6 cycles Option 2: Paclitaxel and carboplatin given once every 3 weeks for 6 cycles. Bevacizumab is added for cycles 2–6 and may be continued by itself for up to 22 cycles.

6 Treatment guide: Stages 2–4

After chemotherapy

After chemotherapy

Treatment after surgery and chemotherapy depends in part on how well chemotherapy worked, and whether the chemotherapy regimen you were treated with included a targeted therapy medicine called bevacizumab (Avastin[®]).

An outcome or improvement related to treatment is called a treatment response. The four main possible treatment responses are described next.

- Complete remission means that there are no signs of cancer on imaging tests, a physical exam, or CA-125 blood tests after treatment.
- Partial remission means that tests show a decrease in the amount of cancer, tumor size,

or CA-125 levels. It means that the cancer improved, but is not completely gone.

- Stable disease is cancer that didn't get better or worse during treatment.
- Progression means that the cancer continued to grow (progress) during or after treatment.

If you were treated with a chemotherapy regimen that included bevacizumab (Avastin[®]), see Guide 6. If the cancer got better or stayed the same, you have the option of continuing treatment with bevacizumab alone as maintenance therapy.

Guide 6. Options after chemotherapy with bevacizumab (Avastin®)

You are in complete or partial remission		
Option 1: Maintenance therapy with bevacizumab (Avastin [®]). Option 2: Maintenance therapy with olaparib (Lynparza [®]) (this option is only for women with <i>BRCA1/2</i> mutations)	•	Begin monitoring for the return of cancer. See <i>When treatment is over</i> on page 50.
The cancer didn't get better or worse (stable disease)		
Maintenance therapy with bevacizumab (Avastin®)	0	Begin monitoring for the return of cancer. See <i>When treatment is over</i> on page 50.
The cancer grew or spread (progression)		
Start treatment for persistent disease. Options include:Enrolling in a clinical trial that is testing newer medicinesStarting supportive care		

• Starting recurrence therapy. Recurrence therapy can include chemotherapy, targeted therapy, immunotherapy, and hormone therapy medicines. See Guides 9 and 11.

6 Treatment guide: Stages 2–4

If you were treated with a chemotherapy regimen that did not include bevacizumab (Avastin[®]), see Guide 7.

Women with *BRCA1/2* mutations who entered complete or partial remission after chemotherapy (with or without bevacizumab) have the option of beginning maintenance therapy with the PARP inhibitor olaparib (Lynparza[®]).

After chemotherapy

If the cancer continued to grow and spread (progress) during chemotherapy (with or without bevacizumab), beginning treatment for persistent disease is recommended.

Begin monitoring for the return of

cancer. See When treatment is

over on page 50.

Guide 7. Options after chemotherapy without bevacizumab (Avastin[®])

You are in complete remission

Option 1: Join a clinical trial.

Option 2: Watch-and-wait (no treatment)

Option 3: Maintenance therapy with olaparib (Lynparza[®]) (for women with *BRCA1/2* mutations)

You are in partial remission

Option 1: Maintenance therapy with olaparib (Lynparza[®]) (for women with *BRCA1/2* mutations). You can begin monitoring for the return of cancer. See *When treatment is over* on page 50.

Option 2: Start treatment for persistent disease. Options include:

- · Enrolling in a clinical trial that is testing newer medicines
- Starting supportive care
- Starting recurrence therapy. Recurrence therapy can include chemotherapy, targeted therapy, immunotherapy, and hormone therapy medicines. See Guides 9 and 11.

The cancer grew or spread (progression)

Start treatment for persistent disease. Options include:

- · Enrolling in a clinical trial that is testing newer medicines
- Starting supportive care
- Starting recurrence therapy. Options for recurrence therapy include chemotherapy, targeted therapy, immunotherapy, and hormone therapy. See Guides 9 and 11.

Other care

Stress and symptom control

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

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

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

Supportive care

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

Next steps

See When treatment is over on page 50 to learn about monitoring for the return of ovarian cancer and what to do if ovarian cancer comes back.

If surgery first isn't an option

Having surgery first may not be an option for some women based on the size and location of the tumor. Having surgery first may also not be a good option for women who are elderly, frail, have trouble doing daily activities, or who have other serious health conditions.

Chemotherapy first

In this case, chemotherapy is recommended first to try to shrink the cancer before surgery. The medical name for this is *neoadjuvant chemotherapy*. It is important that a gynecologic oncologist is involved in this assessment and treatment decision. You will likely have a biopsy to confirm ovarian cancer before starting chemotherapy.

See Guide 5 for the recommended platinum-based chemotherapy regimens recommended by NCCN experts.

If you haven't been referred for genetic counseling and *BRCA1/2* testing yet, they should be done now.

Surgery next, if possible

After a few cycles of chemotherapy, your doctor will check the status of the cancer to see how well chemotherapy worked and if surgery is now possible. The goal of surgery is to remove as much of the cancer as possible, as well as the ovaries, fallopian tubes, and uterus.

If cancer **improved** after three cycles of chemotherapy, surgery is recommended. After surgery, you will likely have more chemotherapy followed by maintenance therapy. If cancer **stayed the same** after 3 cycles of chemotherapy, there are 3 options:

- > Surgery
- Continue chemotherapy (for a total of at least 6 cycles). If the cancer responds to chemotherapy, surgery is recommended next. After surgery, you may have more chemotherapy followed by maintenance therapy. If the cancer doesn't respond, begin treatment for persistent disease.
- > Begin treatment for persistent disease

If the cancer **got worse (progressed)**, begin treatment for persistent disease.

HIPEC

Hyperthermic intraperitoneal chemotherapy (HIPEC) with cisplatin can be considered at the time of surgery for women with stage 3 disease. See page 32 for more information on this type of chemotherapy.

Persistent disease

If cancer continues to grow or spread during chemotherapy or maintenance therapy, it is called persistent disease. Treatment options for persistent ovarian cancer include:

- Join a clinical trial that is testing newer medicines.
- Receive best supportive care. Supportive care is treatment given to relieve the symptoms of cancer or side effects of cancer treatment. It aims to improve quality of life and relieve any discomfort you have. Supportive care may be given alone. It may also be given along with recurrence treatment or treatment within a clinical trial.
- Start recurrence therapy. Options for recurrence therapy include chemotherapy, targeted therapy, immunotherapy, and hormone therapy. See Guides 10 and 11.

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7 When treatment is over

Monitoring for the return of cancer

Follow-up care starts when there are no signs of cancer after treatment. It is also called survivorship care. In addition to monitoring for the return of cancer, follow-up care includes managing side effects, staying connected with your primary care doctor, and living a healthy lifestyle.

Monitoring for the return of cancer

Staying alert for the return of cancer is just as important as treating it. If ovarian cancer does come back, catching it early will give you the best chance of beating it.

When treatment is over, you should continue to see your cancer doctor on a regular basis. During the first two years after treatment, NCCN experts recommend you see your doctor every 2 to 4 months. During the following three years, the visits are spaced out to every 3 to 6 months. After that, one visit per year is recommended.

Many of the tests used for follow-up will be the same as those used to diagnose ovarian cancer. Many of the tests are only done on an as-needed basis. This means that your doctor will decide whether you need a particular test based on any symptoms you may have and other factors.

Genetic counseling is also recommended if it was not done before treatment. Genetic counseling is a discussion with a health expert about the risk for a disease caused by changes in genes. This is recommended because some health problems, including ovarian cancer, can run in families. It is important to know if you have any genetic mutations because you may be a candidate for certain newer targeted therapies.

See Guide 8 for the recommended follow-up schedule and the tests used to monitor for the return of cancer.

Schedule of follow-up visits	Follow-up tests and other care
After treatment, you should have follow-up visits according to the following schedule: • First 2 years: Every 2–4 months • Next 3 years: Every 3–6 months • After 5 years: Once a year	 Physical exam and pelvic exam Imaging of the chest, abdomen, and pelvis with CT, MRI, PET/CT, or PET (as needed) Chest x-ray (as needed) CBC and blood chemistry profile (as needed) CA-125 blood test or other tumor markers (if your levels were high originally) Referral for genetic risk evaluation (if you didn't already have one) Long-term wellness care

Guide 8. Follow-up care after treatment for all stages

Long-term follow-up care

In addition to monitoring for the return of cancer, follow-up care includes managing side effects, staying connected with your primary care doctor, and living a healthy lifestyle.

Cancer survivorship begins on the day you learn you have ovarian cancer. For many survivors, the end of active treatment signals a time of celebration but also of great anxiety. This is a very normal response. 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 longterm side effects, and care of your general health.

Your primary care doctor

After finishing cancer treatment, your primary care doctor will play an important role in your care. Your cancer doctor and primary doctor should work together to make sure you get the follow-up care you need. Your oncologist should develop a survivorship care plan that includes:

- A summary of all cancer-related treatment(s) you've had (surgeries, chemotherapy, radiation, etc.)
- A description of the late- and long-term side effects you could have
- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your primary care physician. The plan should also outline specific responsibilities for both your cancer doctor and your primary care physician
- Recommendations on your overall health and well-being

Living healthy

It is important to keep up with other aspects of your health. There are a few steps you can take that will make a big difference in your overall health, including:

- Getting screened for other types of cancer. Your primary care doctor should tell you what cancer screening tests you should have based on your gender, age, and risk level.
- Getting other recommended health care for your age and gender, such as blood pressure screening, hepatitis C screening, and immunizations (such as the flu shot).
- Maintaining a healthy body weight by exercising at a moderate intensity for at least 30 minutes most days of the week.
- Eating a healthy diet with lots of plant-based foods and drinking little to no alcohol.
- If you are a smoker, quit! Your treatment team will be able to provide you with (or direct you to) resources on quitting smoking.

If cancer comes back

If cancer comes back

The return of cancer after treatment is called a recurrence, or a relapse. Your doctor may suspect that cancer has returned if:

- Your CA-125 levels are going up, but you don't have any symptoms and no cancer can be seen on imaging tests. This is called a **biochemical** relapse.
- Cancer was found on follow-up imaging tests.
 This is called a radiographic relapse.
- You have symptoms of ovarian cancer. Symptoms may include pain or bloating in your pelvis or belly, unexplained weight loss, upset stomach, constipation, trouble eating or feeling full fast, fatigue, and needing to urinate often or urgently. This is called a clinical relapse.

You didn't have chemotherapy

If cancer comes back and you haven't had chemotherapy yet, the cancer is treated the same as if you were newly diagnosed. This means that you will have surgery to remove the cancer and chemotherapy may be given next. The type and extent of surgery depends on how far the cancer has spread.

You had chemotherapy

If you were in complete remission after platinumbased chemotherapy and cancer returned, the treatment options depend on:

- The type of relapse (biochemical, radiographic, and/or clinical), and
- How soon cancer came back after you finished chemotherapy.

Cancer that returns **more than 6 months** after finishing platinum-based chemotherapy is called *platinum-sensitive*.

Cancer that returns **less than 6 months** after finishing platinum-based chemotherapy is called *platinum-resistant*.

First steps

If a relapse is suspected or confirmed, additional testing will be done to gather more information. The tests you may have are described next.

Imaging tests

If you haven't had imaging tests recently, you may have them now. This may include a CT, MRI, PET, or PET/CT scan of your chest, abdomen, and pelvis.

Tumor marker testing

If you haven't already been tested for the following genetic mutations, you should be tested now.

- > BRCA1 and BRCA2 mutations
- MSI or DNA dMMR

An additional tumor marker your doctor may consider testing for is called *homologous recombination deficiency*. Your doctor may consider testing for this tumor marker because treatment with PARP inhibitors (eg, olaparib, rucaparib, and niraparib) may be particularly effective at treating ovarian cancer in women with homologous recombination deficiency. More information on tumor marker tests can be found in Part 2, *Testing for ovarian cancer*.

Treatment of platinum-sensitive and platinumresistant ovarian cancer that returns after treatment is explained on the next pages.

If cancer comes back

Platinum-sensitive ovarian cancer

If you were in complete remission after platinumbased chemotherapy and cancer returned more than 6 months later, the cancer is considered "platinum-sensitive." This means that platinumbased chemotherapy drugs worked well against the cancer. Therefore, you may receive platinum-based chemotherapy again as recurrence treatment. The options for treating platinum-sensitive disease depend on whether you have a biochemical, clinical, or radiographic relapse.

Guide 9. Recurrence treatment for platinum-sensitive epithelial ovarian cancer

		Preferred reg	imens		
		Chemotherapy			Targeted therapy
 Carboplatin and gemcitabine Carboplatin, gemcitabine, and bevacizumab Carboplatin and liposomal doxorubicin, with or without bevacizumab Carboplatin and gemcitabine Cisplatin and gemcitabine Bevacizumab Olaparib Rucaparib 				BevacizumabOlaparibRucaparib	
Other recommended regimens					
Chemoth	ierapy		Targeted therapy		Hormone therapy
 Altretamine Carboplatin and docetaxel Carboplatin and paclitaxel Capecitabine 	 Carboplatin Cisplatin Doxorubicin Ifosfamide Irinotecan Molphology 	 Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Vinorelbine 	Pazopanib	• A (a ex • Le • M • Ta	romatase inhibitors inastrozole, kemestane, letrozole) euprolide acetate legestrol acetate amoxifen

Melphalan

Regimens	usoful ir	cortain	circum	etancos

Chemotherapy	Immunotherapy
 Carboplatin and albumin-bound paclitaxel (for taxane hypersensitivity) Carboplatin and paclitaxel (for women older than 70) 	Pembrolizumab (for MSI-H or dMMR solid tumors)

7 When treatment is over

If cancer comes back

Clinical or radiographic relapse

If you have symptoms of ovarian cancer (a clinical relapse) or imaging tests show that cancer has returned (a radiographic relapse) after chemotherapy, your doctor may want to do surgery to remove all visible cancer before beginning further treatment. This is called cytoreductive surgery. The next treatment options include:

- Enroll in a clinical trial that is testing newer medicines.
- Start recurrence treatment with platinum-based chemotherapy. This option is preferred by NCCN experts if it is your first recurrence. See Guide 9 for the platinum-based recurrence chemotherapy regimens. See Guide 10 for next steps based on how well recurrence treatment works.
- Start treatment with a different type of recurrence therapy (something other than platinum-based chemotherapy). See Guide 9 for options. In this case, radiation therapy may also be given to help with symptoms.

Biochemical relapse

If your CA-125 levels are gradually going up but there are no other signs of recurrence (a biochemical relapse), you have a few options:

- Enroll in a clinical trial that is testing newer medicines.
- Wait until you have symptoms (a clinical relapse) to start recurrence treatment.
- Start recurrence treatment right away with platinum-based chemotherapy. Guide 9 presents the recurrence therapies recommended for platinum-sensitive ovarian cancer. See Guide 10 for next steps based on how well recurrence treatment works.

Response	Treatment options
Complete or partial response	 Option 1: Maintenance therapy with bevacizumab (Avastin[™]) (only if your recurrence treatment included bevacizumab) Option 2: Maintenance therapy with a PARP inhibitor (if you've completed 2 or more rounds of platinum-based therapy). Niraparib (Zejula[™]), olaparib (Lynparza[®]), and rucaparib (Rubraca[®]) are options. Option 3: Watch-and-wait (no treatment)
No response or the cancer got worse	 Option 1: Enroll in a clinical trial that is testing newer medicines. Option 2: More recurrence therapy. See Guide 8 for options. Radiation therapy to help with symptoms may also be given. Option 3: Best supportive care may be given with either of the above options.

Guide 10. After recurrence treatment with platinum-based chemotherapy

7 When treatment is over

If cancer comes back

Platinum-resistant ovarian cancer

If you were in complete remission and cancer returned <u>less than 6 months</u> after you finished platinum-based chemotherapy, the cancer is considered "platinum-resistant." This means that platinum-based chemotherapy drugs like cisplatin and carboplatin did not work very well against the cancer. Therefore, a different type of drug is recommended for recurrence treatment. The options for treating platinum-resistant ovarian cancer include:

- Join a clinical trial that is testing newer medicines.
- Start recurrence therapy. Recurrence therapy can include chemotherapy, hormone therapy, immunotherapy, and targeted therapy medicines. You may also be offered radiation therapy to help with symptoms caused by the cancer.
- Receive best supportive care (can be combined with either of the above options).

Guide 11. Recurrence treatment for platinum-resistant epithelial ovarian cancer

Preferred regimens						
Chemotherapy		Targeted therapy				
 Cyclophosphamide (oral) and bevacizumab Docetaxel Etoposide (oral) Gemcitabine 	 Liposomal doxorubicin and bevacizumab Paclitaxel (weekly) Paclitaxel (weekly) and bevacizumab Topotecan Topotecan/bevacizumab 	BevacizumabOlaparibRucaparib				

041			
Other	recommend	led redi	mens

Chemothe	rapy		Targeted therapy	Hormone therapy
 Altretamine Capecitabine Cyclophosphamide Doxorubicin Ifosfamide Irinotecan 	 Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound 	 Pemetrexed Sorafenib and topotecan Vinorelbine 	Pazopanib	 Aromatase inhibitors (anastrozole, exemestane, letrozole) Leuprolide acetate Megestrol acetate Tamoxifen

Regimens useful in certain circumstances

Immunotherapy

Pembrolizumab (for MSI-H or dMMR solid tumors)



SNAPSHOT: Hypersensitivity reactions

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

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

8 Making treatment decisions

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8 Making treatment decisions

Finding out you have cancer can be very stressful. While absorbing the fact that you have cancer, you also must learn about tests and treatments. In addition, the time you have to decide on a treatment plan may feel short. This chapter addresses ways to assist you when deciding on a treatment plan.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. However, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works best for you when it comes to your personal and health needs.

Questions to ask your doctors

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn't clear. You can also get copies of your medical records. It may be helpful to have a family member or friend with you at these visits to listen carefully and even take notes. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions below are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.

Questions to ask your doctors about testing

- 1. What tests will I have?
- 2. Where will the tests take place? Will I have to go to the hospital?
- 3. How long will it take? Will I be awake?
- 4. Will any test hurt?
- 5. What are the risks?
- 6. How do I prepare for testing?
- 7. Should I bring a list of my medications?
- 8. Should I bring someone with me?
- 9. How soon will I know the test results?
- 10. Who will explain the test results to me?
- 11. Can I have a copy of the test results and pathology report?
- 12. Who will talk with me about the next steps? When?

Questions to ask your doctors about treatment

- 1. What treatments do you recommend?
- 2. Will I have more than one treatment?
- 3. What are the risks and benefits of each treatment? What about side effects?
- 4. Will my age, general health, and other factors affect my treatment choices?
- 5. Would you help me get a second opinion?
- 6. How soon should I start treatment? How long does treatment take?
- 7. Where will I be treated? Will I have to stay in the hospital or can I go home after each treatment?
- 8. What can I do to prepare for treatment?
- 9. What symptoms should I look out for during treatment?
- 10. How much will the treatment cost? How can I find out how much my insurance company will cover?
- 11. How likely is it that I'll be cancer-free after treatment?
- 12. What is the chance that the cancer will come back?
- 13. What should I do after I finish treatment?
- 14. Are there supportive services that I can get involved in? Support groups?

Questions to ask your doctors about clinical trials

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

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

- 1. Are you board-certified? If yes, in what area?
- 2. How many patients like me have you treated?
- 3. How many procedures like the one you're suggesting have you done?
- 4. Is this treatment a major part of your practice?
- 5. How many of your patients have had complications?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions about which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Getting a second opinion

Even if you like and trust your doctor, it may be helpful to get a second opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. You want to know about out-of-pocket costs for 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. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.
- If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with ovarian cancer. If your hospital or community doesn't have support groups for women with ovarian cancer, check out the websites on the next page.

You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and those with children so they can connect and get support.

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a second opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.

What to remember...

- Every treatment option has benefits and risks. Consider these when deciding which option is best for you.
 - Talking to others may help identify benefits and risks you haven't thought of.

Websites

FORCE: Facing Our Risk of Cancer Empowered

facingourrisk.org

National Ovarian Cancer Coalition

ovarian.org

Ovarcome

ovarcome.org

Ovarian & Breast Cancer Alliance of Washington State

knowthesymptoms.org

Ovarian Cancer Research Alliance

ocrahope.org

Sharsheret

sharsheret.org



Words to know

abdomen

The belly area between the chest and pelvis.

adjuvant treatment

Treatment given after the main treatment used to rid the body of disease.

ascites

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

β-hCG

beta-human chorionic gonadotropin

bilateral salpingo-oophorectomy (BSO)

Surgery to remove both ovaries and both fallopian tubes.

biochemical relapse

A rise in CA-125 levels signals that cancer has come back after treatment.

biopsy

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

blood chemistry profile

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

borderline epithelial tumor (low malignant potential [LMP])

A tumor formed by abnormal cells that start in the epithelial cells of the ovary. This tumor type is slow growing and does not invade other tissue.

BRCA1 or BRCA2 genes

Coded information in cells that help to prevent tumor growth by fixing damaged cells and helping cells grow normally. Abnormal changes within these genes increases the chances of developing breast and ovarian cancer.

cancer antigen 125 (CA-125)

A protein with sugar molecules on it that is made by ovarian cancer cells and normal cells.

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.

cancer staging

The process of rating and describing the extent of cancer in the body.

capsule

A thin layer of tissue that surrounds an organ—like the skin of an apple.

CEA

carcinoembryonic antigen

cell subtype

Smaller groups that a type of cancer is divided into based on how the cancer cells look under a microscope.

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.

chest x-ray

A test that uses x-rays to make pictures of the inside of the chest.

clear cell

One of the four main cell subtypes of ovarian cancer.

clinical relapse

Physical signs or symptoms signal that cancer has come back after treatment.

clinical trial

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

combination regimen

The use of two or more drugs.

complete blood count (CBC)

A test of the number of blood cells.

complete response

All signs and symptoms of cancer are gone after treatment.

completion surgery

Surgery to remove the remaining ovary, fallopian tube, uterus, and all cancer that can be seen.

computed tomography (CT) scan

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

Words to know

contrast

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

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.

dMMR mismatch repair deficient

DNA deoxyribonucleic acid

epithelial cells

Cells that form the outer layer of tissue around organs in the body.

epithelial ovarian cancer

Cancer that starts in the cells that form the outer layer of tissue around the ovaries.

fallopian tube

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

fertility-sparing surgery

Surgery that only removes one ovary and fallopian tube so that a woman can still have babies.

FNA

fine-needle aspiration

gastrointestinal (GI) evaluation

A test to view the organs that food passes through when you eat.

gastrointestinal tract

The group of organs that food passes through when you eat.

general anesthesia

A controlled loss of wakefulness from drugs.

genetic counseling

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

genetic counselor

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

genetic testing

Tests to look for changes in coded instructions (genes) that increase the risk for a disease.

germ cell

Reproductive cells that become eggs in women and sperm in men.

gynecologic oncologist

A surgeon who's an expert in cancers that start in a woman's reproductive organs.

hereditary ovarian cancer

Ovarian cancer caused by abnormal coded information in cells that is passed down from parent to child.

hormone

Chemicals in the body that activate cells or organs.

hormone therapy

Treatment that stops the making or action of hormones in the body.

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 chemotherapy drugs that have been warmed up.

hysterectomy

Surgery to remove the uterus.

imaging test

Tests that make pictures (images) of the inside of the body.

implant

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

infusion

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

intraperitoneal (IP)

Given directly into the belly (abdomen) through a small tube.

intraperitoneal (IP) chemotherapy

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

Words to know

intravenous (IV) Given by a needle or tube inserted into a vein.

intravenous (IV) chemotherapy

Chemotherapy drugs given through a needle or tube inserted into a vein.

invasive implant

Cancer cells that broke away from the first tumor and are growing into (invading) supporting tissue of nearby organs.

laparotomy

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

LCOH

less common ovarian histologies

LDH lactate dehydrogenase

LHRH luteinizing hormone-releasing hormone

liver function test

A blood test that measures chemicals that are made or processed by the liver to check how well the liver is working.

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.

lymph vessels

Small tubes that carry lymph—a clear fluid with white blood cells that fight infection and disease—throughout the body.

Lynch syndrome

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

magnetic resonance imaging (MRI) scan

A test that uses radio waves and powerful magnets to make pictures of the inside of the body.

maintenance treatment

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.

menstrual cycle

Changes in the womb and ovaries that prepare a woman's body for pregnancy.

metastases

Tumors formed by cancer cells that have spread from the first tumor to other parts of the body.

metastasis

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

microscope

A tool that uses lenses to see very small things the eyes can't.

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.

MMMT

malignant mixed Müllerian tumors

MMR

mismatch repair

MSI

microsatellite instability

MSI-H

microsatellite instability-high

mutation

An abnormal change in the instructions in cells for making and controlling cells.

neuropathy

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

noninvasive implant

Cancer cells that broke away from the first tumor and are growing on the surface of nearby organs, but are not growing into (invading) tissue.

observation

A period of testing to watch for cancer growth.

omentum

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

ovaries

The pair of organs in women that make eggs for reproduction (making babies) and make hormones.

ovary

One of a pair of organs in women that make eggs for reproduction (making babies) and make hormones.

pathologist

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

pelvic exam

A medical exam of the female organs in the pelvis.

pelvis

The body area between the hip bones.

peritoneal cavity

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

peritoneal washing

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

peritoneum

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

persistent disease

Cancer that stayed the same—didn't get better or worse—during treatment.

platinum agent

A cancer drug that is made with platinum. These drugs damage DNA in cells, which stops them from making new cells and causes them to die.

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.

poly (ADP-ribose) polymerase (PARP) inhibitor

A type of targeted therapy that blocks a protein in cells called PARP that helps repair damaged DNA.

positron emission tomography (PET) scan

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

positron emission tomography (PET)/computed tomography (CT) scan

A test that uses a sugar radiotracer and x-rays from many angles to view the shape and function of organs and tissues inside the body.

primary tumor

The first mass of cancer cells in the body.

prognosis

The likely or expected course and outcome of a disease.

radiographic relapse

Imaging tests show signs that cancer has come back after treatment.

radiologist

A doctor who's an expert in reading imaging tests—tests that make pictures of the inside of the body.

recurrence

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

recurrence treatment

Treatment that is given after prior treatments failed to kill all the cancer or keep it away.

regimen

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

relapse

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

reproductive system

The group of organs that work together to make babies. In women, this includes the ovaries, fallopian tubes, uterus, cervix, and vagina.

serous

The most common cell subtype of ovarian cancer.

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Words to know

stromal cell

Cells that form the connective and supporting tissues that hold the ovary together.

sugar radiotracer

A form of sugar that is put into your body and lets off a small amount of energy that is absorbed by active cells.

supportive care

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

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 cancer drug that blocks certain cell parts to stop a cell from dividing into two cells.

TKI

tyrosine kinase inhibitor

treatment response

An outcome or improvement related to treatment.

tumor

An abnormal mass formed by the overgrowth of cells.

tumor marker

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

ultrasound

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

unilateral salpingo-oophorectomy (USO)

Surgery that removes one ovary and the attached fallopian tube.

uterus

The female organ where babies grow during pregnancy. Also called womb.

vagina

The hollow, muscular tube in women through which babies are born.

vein

A blood vessel that carries blood back to the heart from all parts of the body.

washings

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

white blood cell

A type of blood cell that helps fight infections in the body.

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

Fred & Pamela Buffett Cancer Center Omaha, Nebraska 800.999.5465 <u>nebraskamed.com/cancer</u>

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

City of Hope National Medical Center Los Angeles, California 800.826.4673 cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center Massachusetts General Hospital Cancer Center *Boston, Massachusetts* 877.332.4294 <u>dfbwcc.org</u> <u>massgeneral.org/cancer</u>

Duke Cancer Institute Durham, North Carolina 888.275.3853 dukecancerinstitute.org

Fox Chase Cancer Center Philadelphia, Pennsylvania 888.369.2427 foxchase.org

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 877.585.0303 huntsmancancer.org

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance Seattle, Washington 206.288.7222 • <u>seattlecca.org</u> 206.667.5000 • <u>fredhutch.org</u> The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Baltimore, Maryland 410.955.8964 hopkinskimmelcancercenter.org

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

Mayo Clinic Cancer Center Phoenix/Scottsdale, Arizona Jacksonville, Florida Rochester, Minnesota 800.446.2279 • Arizona 904.953.0853 • Florida 507.538.3270 • Minnesota mayoclinic.org/cancercenter

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

Moffitt Cancer Center Tampa, Florida 800.456.3434 moffitt.org

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

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

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

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine *St. Louis, Missouri* 800.600.3606 <u>siteman.wustl.edu</u> St. Jude Children's Research Hospital The University of Tennessee Health Science Center *Memphis, Tennessee* 888.226.4343 • <u>stjude.org</u> 901.683.0055 • <u>westclinic.com</u>

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

UC San Diego Moores Cancer Center La Jolla, California 858.657.7000 <u>cancer.ucsd.edu</u>

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

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

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

The University of Texas MD Anderson Cancer Center Houston, Texas 800.392.1611 mdanderson.org

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

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 800.811.8480 <u>vicc.org</u>

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

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