

TREATMENT UPDATE:

Ovarian Cancer

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Treatment Update: Ovarian Cancer

TABLE OF CONTENTS

| | |
|---|----|
| Introduction..... | 4 |
| Stages of Ovarian Cancer | 5 |
| Treatment Options..... | 7 |
| Treatment Approaches Being Studied | 11 |
| The Importance of Clinical Trials | 12 |
| Treatment Side Effects..... | 13 |
| Communicating With Your Health Care Team..... | 18 |
| CancerCare’s Free Support Services and Programs.. | 20 |
| Frequently Asked Questions..... | 21 |
| Resources..... | 23 |

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Each year, over 22,000 women in the United States are diagnosed with ovarian cancer.

Ovarian cancer affects the ovaries and fallopian tubes. The ovaries are organs which produce the female reproductive cells (ova). The ovaries, each about the size of an almond, are located beside the uterus on each side of the lower abdomen. The fallopian tubes carry eggs from the ovaries to the uterus.

There are more than 30 types and subtypes of ovarian cancer. Most experts group ovarian cancers into three major categories, based on the type of cells from which they were formed:

- **Epithelial tumors** arise from cells that line or cover the ovaries and/or fallopian tubes. This is the most common category of ovarian cancer, accounting for approximately 90 percent of cases.
- **Germ cell tumors** originate from cells that are destined to form eggs within the ovaries.
- **Sex cord-stromal cell tumors** begin in the connective cells that hold the ovaries together and produce female hormones.

In recent years, the molecular analysis of tumors has led to refinements in ovarian cancer classifications, providing insights that may lead to the development of new therapies.

Stages of Ovarian Cancer

To plan the best treatment, your doctor needs to know the stage of your cancer, which describes whether and how much it has spread to nearby tissues and organs. Since ovarian cancer is often discovered when it has already advanced, treatment usually begins with surgery, in which the surgeon removes as much of the cancer as possible. After surgery, samples of the tumor and tissues from the pelvis and abdomen are put under a microscope to stage the cancer.

- **Stage 1:** The cancer is found only in the ovary (or ovaries).
- **Stage 2:** The cancer has spread into other parts of the pelvis, such as the bladder or lower colon.
- **Stage 3:** The cancer has spread beyond the pelvis into the lining of the abdomen or the lymph nodes, which are the small “filtering stations” that remove waste and fluids from tissues and organs and help fight infections in the body.
- **Stage 4:** The cancer has spread into more distant organs, such as the liver or lungs.



Other tests may be performed to help determine the stage of the cancer, such as:

- **CT scan (computerized tomography)**, which combines X-ray images taken from different angles with computer processing to create cross-sectional images of organs and tissues.
- **MRI (magnetic resonance imaging)**, a technique that uses a magnetic field and radio waves to create detailed images of the organs and tissues within the body.
- **PET scan (positron emission tomography)**, a functional imaging test that uses a radioactive drug to detect cancer.

Before surgery, a blood test may be performed to measure your levels of CA-125, a sugar-related protein found in the blood. Women with ovarian cancer often have high levels of this protein, but it is not the most reliable indicator that a tumor is present. CA-125 can be absent when cancer is present, and levels can be high when no cancer exists. Still, doctors use CA-125 as a gauge, and blood tests to measure CA-125 may also be performed post-surgery and during subsequent treatment (to determine response to the treatment).



Treatment Options

Surgery

Treatment for ovarian cancer usually begins with surgery, in which the surgeon removes as much of the cancer as possible. In many cases, a total hysterectomy (removal of the uterus, fallopian tubes and ovaries) is performed. Experts recommend that the surgery be performed by a gynecologic oncologist—a specialist who has training and experience in treating and staging ovarian cancer.

Gynecologic oncologists are also more likely than general surgeons and gynecologists to optimally “debulk” the cancer. Optimal debulking means that, after surgery, no visible tumor remains or the size of the remaining tumor is less than one centimeter (less than half an inch). Suboptimal debulking is when more than one centimeter of tumor is left behind. Whether the surgery is optimal or suboptimal is a factor in guiding future treatment options.

Chemotherapy

After surgery, almost all women are treated with intravenous (delivered into a vein) chemotherapy. Usually, this chemotherapy combines two or more drugs, as this seems to be more effective in stopping the progression of ovarian cancer than administering one drug alone.

The standard approach is the combination of a platinum compound, such as cisplatin or carboplatin, and a taxane (a type of drug that blocks cell growth by stopping cell division), such as paclitaxel or docetaxel. The targeted therapy bevacizumab, a treatment that affects blood supply to tumors, may be added to the chemotherapy regimen.

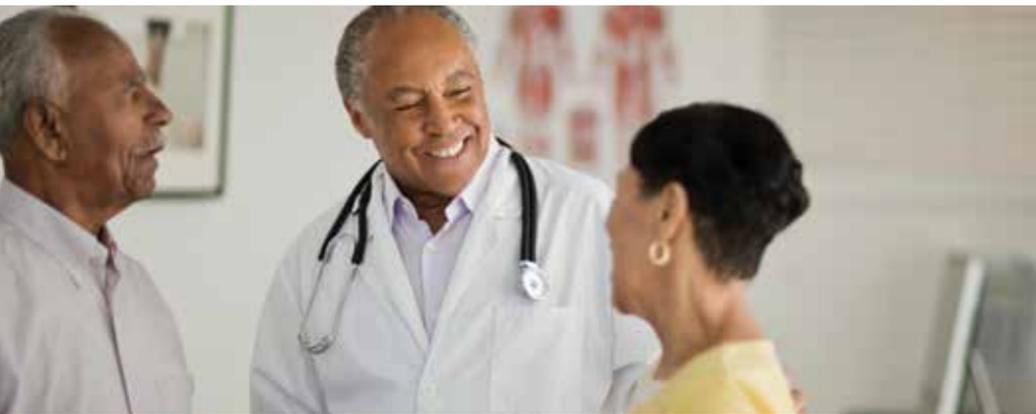
The typical course of chemotherapy involves six cycles (a cycle is a schedule of regular doses of a drug, followed by a rest period), although cycles vary depending on the drugs being used.

In addition to receiving intravenous chemotherapy, women whose debulking surgery was optimal may also be offered intraperitoneal (IP) chemotherapy. This treatment delivers a concentrated dose of chemotherapy directly to the cancer cells through a tube placed in the abdomen.

Following debulking surgery and chemotherapy

Most women who have had debulking surgery followed by six cycles of chemotherapy go into complete remission. This is when the cancer seems to have disappeared from the body and no test currently available can detect any remaining cancer.

For women in complete remission, treatment may be stopped or may be continued as consolidation (maintenance) therapy, which is treatment given after the cancer has disappeared following the initial therapy. The goal of consolidation therapy is to maintain the remission and delay or prevent a relapse. Targeted therapies, such as bevacizumab and PARP inhibitors, may be used as consolidation therapy (see next section for information on targeted therapy).



Women whose ovarian cancer does not go into remission or whose cancer returns less than six months after the first full course of chemotherapy are usually treated with chemotherapy drugs other than what they received during their initial treatment. Those drugs include pegylated liposomal doxorubicin (PLD), topotecan and gemcitabine. The option of a clinical trial should be considered as this may provide access to new therapies.

If ovarian cancer returns more than six months after the first full course of chemotherapy, a woman may be retreated with the chemotherapy carboplatin in combination with paclitaxel, PLD or gemcitabine.

Targeted Therapy

Targeted therapies are designed to target the specific cell mechanisms that are important for the growth and survival of tumor cells. The following targeted therapies have been approved by the United States Food and Drug Administration (FDA) for the treatment of ovarian cancer:

- **Bevacizumab (Avastin).** Bevacizumab works by preventing the growth of new blood vessels that feed tumors. Bevacizumab was initially approved, in combination with chemotherapy, for the treatment of advanced ovarian cancer that has recurred (come back) after previous therapy. In June 2018, the FDA approved bevacizumab for the treatment of epithelial ovarian cancer, in combination with carboplatin and paclitaxel, for the treatment of Stage 3 or Stage 4 ovarian cancer after initial surgery.

- **PARP inhibitors.** PARPs are enzymes that regulate cell survival and cell death. PARP inhibitors are designed to destroy cancer cells by preventing them from repairing their damaged DNA. There are three PARP inhibitors approved for the treatment of ovarian cancer, under specific circumstances:

- **Olaparib (Lynparza).** In 2014, the FDA approved olaparib for the treatment of previously treated, advanced ovarian cancer associated with defective BRCA genes, as detected by an FDA-approved test. In December 2018, the approval was extended to include the first-line (initial) treatment of BRCA-mutated advanced ovarian cancer.
- **Rucaparib (Rubraca).** Rucaparib was approved by the FDA in 2016 to treat women with advanced ovarian cancer who have been treated with two or more chemotherapies and have a specific gene mutation called “deleterious BRCA.” In April 2018, the FDA approved rucaparib as a consolidation therapy for women with recurrent (returned) epithelial ovarian cancer whose cancer has responded to platinum-based chemotherapy.
- **Niraparib (Zejula).** In 2017, niraparib was approved for the treatment of recurrent epithelial ovarian cancer for patients whose tumors have completely or partially shrunk in response to platinum-based chemotherapy.



Treatment Approaches Being Studied

There are a number of new approaches being tested for the treatment of ovarian cancer, including:

- **Overcoming platinum resistance.** When the drugs cisplatin and carboplatin stop working, the cancer is said to be “platinum resistant.” Researchers are looking for ways to make the cancer sensitive to these drugs again.
- **Targeted therapy.** Targeted therapies being studied include additional PARP inhibitors and the VEGFR-inhibitor pazopanib (Votrient). VEGFR-inhibitors target and bind to receptors on the inside of cancer cells, blocking the growth of new blood vessels that feed tumors.
- **Immunotherapy.** Immunotherapy is a treatment approach that uses certain parts of the immune system to fight illnesses such as cancer and has shown promising results in the treatment of ovarian cancer. One immunotherapy being studied, for use in combination with a PARP inhibitor, interferes with a molecular “brake” known as PD-1 that prevents the body’s immune system from attacking tumors.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the safety and effectiveness of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Many clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- Participation is voluntary and does not affect your access to treatment in other settings. You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to maintain your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used. They can include:

- Fatigue
- Nausea or vomiting
- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding (from having a low platelet count)
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Chemotherapy can cause changes in the way food and liquids taste, including causing an unpleasant metallic taste in the mouth. Many people find that switching to plastic utensils helps. It may also help to avoid eating or drinking anything that comes in a can, and to use enamel-coated pots and pans for food preparation.

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. Electrolytes are body salts that must stay in balance for cells to work properly.

Managing loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. He or she may also think of questions to ask your doctor or

remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you. If you have a mobile device, ask if you can use it to take notes. Keeping notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your ovarian cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

CancerCare's Free Support Services and Programs

It is very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

CancerCare® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.



Frequently Asked Questions

Q: I was recently diagnosed with ovarian cancer, and I have large tumors in my abdominal cavity. Before the surgery, my oncologist wants me to have chemotherapy to shrink the tumors. Is this a common practice?

A: Chemotherapy delivered before surgery—known as neoadjuvant chemotherapy—can be an option for some women, including those whose tumors are likely to be difficult to remove and those who may not be able to physically withstand surgery. It's always best to consult a gynecologic oncologist who can confirm what the best option is for you—whether to have surgery first or chemotherapy first. Most women who undergo neoadjuvant chemotherapy still benefit from at least one attempt to have their tumors removed surgically.

Q: Why do some treatments work for some women with ovarian cancer but not for others?

A: This is most likely due to differences in the genetic makeup of each woman's tumor. In recent years, scientists have learned that the tumors of people with the same type and stage of cancer can have different genetic characteristics that may affect how they respond to treatment. In some cases, having an understanding of a tumor's genetic makeup helps doctors better select treatments that are more likely to work. (This is called "precision" or "personalized" medicine.) The goal of ongoing research is to identify all of the genetic characteristics of tumors, in order to treat them more effectively.

Q: My doctor suggested I see a genetic counselor. Why?

A: The Society of Gynecologic Oncology (SGO) recommends that women diagnosed with ovarian cancer undergo genetic counseling and testing. Genetic counseling can help women make informed decisions about genetic testing. In a genetic counseling session for ovarian cancer, the counselor will typically collect a detailed family and medical history and discuss genetic mutations, such as those in BRCA1 and BRCA2 genes, which can increase the chance of developing ovarian cancer.

Q: I've been diagnosed with ovarian cancer. Because it's a reproductive cancer, should I avoid foods high in estrogen?

A: Foods high in estrogen include tofu, tempeh, soy milk, soybeans, dried fruits, peas and bran cereals. There is no evidence that these foods increase the risk or treatment of ovarian cancer if eaten in moderation as part of a healthy diet. Excessive amounts of these and other estrogen-rich foods should be avoided, and estrogen supplements should not be taken.

Resources

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American Cancer Society

800-227-2345
www.cancer.org

Cancer.Net

Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute

800-422-6237
www.cancer.gov

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship

877-622-7937
www.canceradvocacy.org

National Ovarian Cancer Coalition

888-OVARIAN (888-682-7426)
www.ovarian.org

Ovarian Cancer Research Alliance (OCRA)

800-873-9569
www.ocrahope.org

CLINICAL TRIALS WEBSITES

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