



OVARIAN CANCER

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ABSTRACT:

Poly (ADP-ribose) polymerase inhibitors (PARP inhibitors) are targeted therapy drugs that block DNA repair and may cause cancer cells to die. Olaparib, rucaparib, and niraparib are PARP inhibitors that may be used as maintenance therapy to treat certain types of ovarian epithelial cancer, fallopian tube cancer, or primary peritoneal cancer that have recurred. Veliparib is a PARP inhibitor that is being studied in combination with chemotherapy to treat advanced ovarian cancer. New types of treatment are being tested in clinical trials. This summary section describes treatments that are being studied in clinical trials. It may not mention every new treatment being studied. Information about clinical trials is available from the NCI website. Radiation therapy Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. Some women receive a treatment called intraperitoneal radiation therapy, in which radioactive liquid is put directly in the abdomen through a catheter. Intraperitoneal radiation therapy is being studied to treat advanced ovarian cancer.

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This cancer treatment is a type of biologic therapy. Vaccine therapy is a cancer treatment that uses a substance or group of substances to stimulate the immune system to find the tumor and kill it. Vaccine therapy is being studied to treat advanced ovarian cancer. Treatment for ovarian epithelial, fallopian tube, and primary peritoneal cancer may cause side effects. For information about side effects caused by treatment for cancer, see our Side Effects page. Patients may want to think about taking part in a clinical trial. For some patients, taking part in a clinical trial may be the best treatment choice. Clinical trials are part of the cancer research process. Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment. Many of today's standard treatments for cancer are based on earlier clinical trials. Patients who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment. Patients who take part in clinical trials also help improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward. Patients can enter clinical trials before, during, or after starting their cancer treatment

KEYWORDS:

BRCA1, BRCA2.



INTRODUCTION

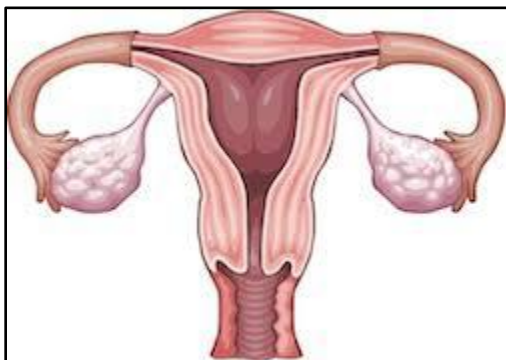
Ovarian cancer is a growth of cells that forms in the ovaries. The cells multiply quickly and can invade and destroy healthy body tissue. The female reproductive system contains two ovaries, one on each side of the uterus. The ovaries — each about the size of an almond — produce eggs (ova) as well as the hormones estrogen and

progesterone. Ovarian cancer treatment usually involves surgery and chemotherapy. The existing screening tests have a low predictive value contributing further to this misery. Detailed gynecological evaluation along with transvaginal ultrasound and laboratory marker like cancer antigen-125 (CA-125) assay are the key early detection

strategies which have shown no significant beneficial effect in the morbidity or mortality of this cancer. The standard line of care treatment includes surgery and platinum-based chemotherapy; however, anti-angiogenic bevacizumab and Poly(ADP-ribose) polymerase (PARP) inhibitors have gained momentum in the management of this gynecological malignancy in the past decade.

A high rate of recurrence following the initial treatment has been observed. Most of these relapsed cases are less curable and known to have an increased incidence of treatment failures. Hence, effective prevention and detection strategies and new treatment modalities based on a better understanding of molecular characterization of this cancer are the need of the hour. This article reviews the epidemiology, risk factors of ovarian cancer and also highlights the evaluation and multidisciplinary approach in the management of this condition, along with a discussion of a few of the recent ongoing trials.

The risk of ovarian cancer increases with age. Most cases of ovarian cancer develop after menopause.] It is also more common in women who have ovulated more over their lifetime. This includes those who have never had children, those who began ovulation at a younger age and those who reach menopause at an older age. Other risk factors include hormone therapy after menopause, fertility medication, and obesity. Factors that decrease risk include hormonal birth control, tubal ligation, pregnancy, and breast feeding. About 10% of cases are related to inherited genetic risk; women with mutations in the genes BRCA1 or BRCA2 have about a 50% chance of developing the disease. Some family cancer syndromes such as hereditary nonpolyposis colon cancer and Peutz-Jeghers syndrome also increase the risk of developing ovarian cancer. Epithelial ovarian carcinoma is the most common type of ovarian cancer, comprising more than 95% of cases. There are five main subtypes of ovarian carcinoma, of which high-grade serous carcinoma (HGSC) is the most common. Less common types of ovarian cancer include germ cell tumors] and sex cord stromal tumors. A diagnosis of ovarian cancer is confirmed through a biopsy of tissue, usually removed during surgery.



SYMPTOMS-

When ovarian cancer first develops, it might not cause any noticeable symptoms. When ovarian cancer symptoms happen, they're usually attributed to other, more common conditions.

Signs and symptoms of ovarian cancer may include:

- Abdominal bloating or swelling
- Quickly feeling full when eating
- Weight loss
- Discomfort in the pelvic area
- Fatigue
- Back pain
- Changes in bowel habits, such as constipation
- A frequent need to urinate

Ovarian cancer may cause several signs and symptoms. Women are more likely to have symptoms if the disease has spread, but even early-stage ovarian cancer can cause them. The most common symptoms include:

- Bloating
- Pelvic or abdominal (belly) pain
- Trouble eating or feeling full quickly
- Urinary symptoms such as urgency (always feeling like you have to go) or frequency (having to go often)

These symptoms are also commonly caused by benign (non-cancerous) diseases and by cancers of other organs. When they are caused by ovarian cancer, they tend to be *persistent* and a *change from normal* – for example, they occur more often or are more severe. These symptoms are more likely to be caused by other conditions, and most of them occur just about as often in women who don't have ovarian cancer. But if you have these symptoms more than 12 times a month, see your doctor so the problem can be found and treated if necessary.

OTHERS SYMPTOMS OF OVARIAN CANCER CAN INCLUDE:

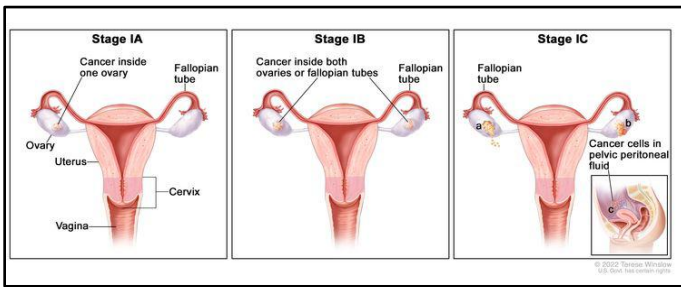
- Fatigue (extreme tiredness)
- Upset stomach
- Back pain
- Pain during sex
- Constipation
- Changes in a woman's period, such as heavier bleeding than normal or irregular bleeding
- Abdominal (belly) swelling with weight loss

WHAT ARE THE FOUR STAGES OF OVARIAN CANCER?

There are four stages of cancer of the ovaries, fallopian tubes and peritoneum, ranging from early to advanced cancer.

STAGE 1 - Stage I ovarian cancer is considered an early cancer.

This stage is divided into three sub stages, A, B, and C:



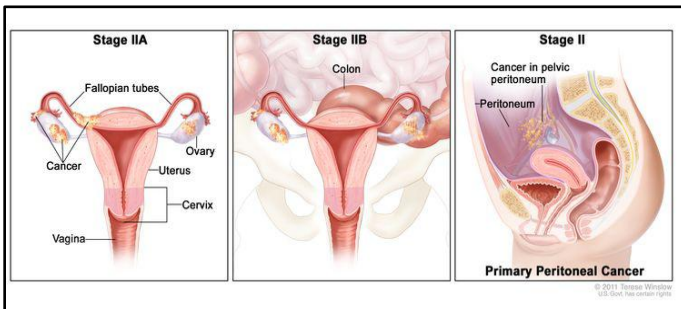
Stage IA: cancer cells are present in one ovary or fallopian tube.

Stage IB: cancer cells are present in both ovaries, or in both fallopian tubes.

Stage IC: cancer cells are present in one or both ovaries or fallopian tubes, and one of the following:

- The outside of the ovaries or fallopian tubes has cancer cells;
- The covering of the ovary, called the capsule, has broken open; or
- Cancer cells are found in your peritoneal cavity, its tissue lining, or fluid from your abdomen.

STAGE 2- This stage is divided into two substages, A and B:



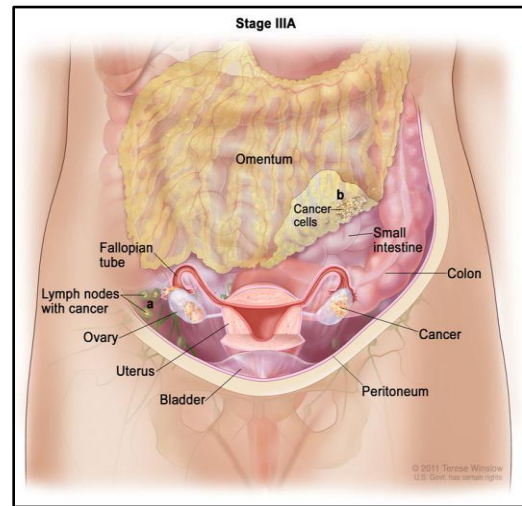
Stage IIA: cancer has spread from the ovary or ovaries to the fallopian tubes and/or the uterus, or it has spread from the fallopian tubes to the ovaries and/or uterus.

Stage IIB: cancer has spread in the peritoneal cavity to your bladder, colon, or rectum.

STAGE 3- This stage is divided into three substages, A, B, and C:

Stage IIIA is defined in one of two ways:

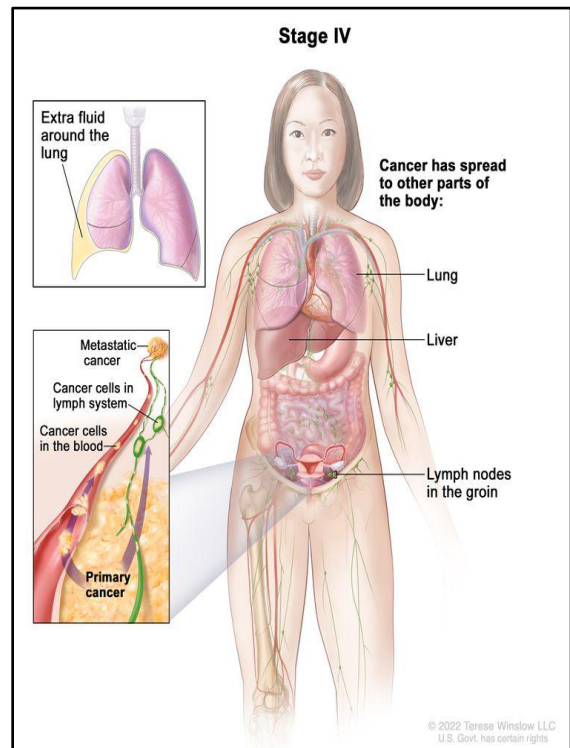
1. cancer cells have spread to the closest lymph nodes, called the retroperitoneal lymph nodes.
2. The surgeon cannot see the cancer with the naked eye, but using a microscope to examine the samples, the pathologist can see that the cancerous cells have spread to the outside the pelvis to the peritoneum (lining). The cancer may also have spread to nearby lymph nodes.



Stage IIIB: cancer inside the peritoneum can be seen by the surgeon, but is still 2 centimeters or smaller. The cancer has also spread outside the pelvis. It may have spread to nearby lymph nodes.

Stage IIIC: the cancer has grown to 2 centimeters in diameter or larger, and has spread to the peritoneum outside the pelvis. It may also have spread the outside of the liver and/or the spleen, as well as nearby lymph nodes.

STAGE 4- There are two substages, A and B:



Stage IVA: cancer cells are found in extra fluid that has built up around the lungs.

Stage IVB: cancer has spread to organs and tissues outside the abdomen, including lymph nodes in the groin.

TYPES OF OVARIAN CANCER

The type of cell where the cancer begins determines the type of ovarian cancer you have and helps your doctor

determine which treatments are best for you. Ovarian cancer types include:

TYPES OF OVARIAN CANCER-

Epithelial ovarian cancer. This type is the most common. It includes several subtypes, including serous carcinoma and mucinous carcinoma.

- **Stromal tumors.** These rare tumors are usually diagnosed at an earlier stage than other ovarian cancers.
- **Germ cell tumors.** These rare ovarian cancers tend to occur at a younger age.

CAUSES- It's not clear what causes ovarian cancer, though doctors have identified things that can increase the risk of the disease.

Doctors know that ovarian cancer begins when cells in or near the ovaries develop changes (mutations) in their DNA. A cell's DNA contains the instructions that tell the cell what to do. The changes tell the cells to grow and multiply quickly, creating a mass (tumor) of cancer cells. The cancer cells continue living when healthy cells would die. They can invade nearby tissues and break off from an initial tumor to spread (metastasize) to other parts of the body.

Some factors that can increase your risk of ovarian cancer include:

- age (risk increases for women over 50)
- family history of ovarian, breast or bowel cancer
- changes in the genes BRCA1 or BRCA2
- being of Ashkenazi Jewish descent
- early onset of periods (before 12 years) and late menopause
- women who have not had children or had their first child after the age of 35
- using oestrogen only hormone replacement therapy or fertility treatment.

Some factors that may reduce the risk of developing ovarian cancer include using the oral contraceptive pill for several years, having your fallopian tubes tied (or removed), having children before the age of 35 and breastfeeding.

DIAGNOSIS OF OVARIAN CANCER

If you are experiencing possible symptoms of ovarian cancer your doctor may suggest several tests or scans to look for cysts, tumours or other changes. These may include:

PHYSICAL EXAMINATION

In which the doctor will check your abdomen for any lumps and do an internal vaginal examination.

BLOOD TESTS

To check for a common tumour marker for ovarian cancer, CA125.

PELVIC ULTRASOUND

A pelvic ultrasound uses echoes from soundwaves to create a picture of your ovaries and uterus.

CT SCAN

A CT (computerised tomography) scan uses x-rays to take images of the inside of your body to check for cancer and to see if it has spread.

PET SCAN

A PET (positron emission tomography) scan highlights abnormal tissues in the body.

COLONOSCOPY

A colonoscopy, which is a bowel examination to ensure that symptoms are not caused by a bowel problem.

These tests can show if there are any abnormalities but a biopsy (taking a tissue sample) is the only way to confirm a cancer diagnosis.

TREATMENT OF OVARIAN CANCER- DIAGNOSIS OF OVARIAN CANCER

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PHYSICAL EXAMINATION

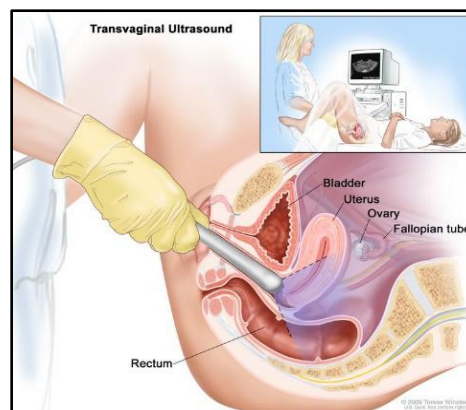
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PREVENTION- There is no known way to prevent most ovarian cancers. But there are things you can do that might lower your risk.

TREATMENT OPTION OVERVIEW

KEY POINTS

- There are different types of treatment for patients with ovarian epithelial cancer.
- Three kinds of standard treatment are used.
 - Surgery
 - Chemotherapy
 - Targeted therapy
- New types of treatment are being tested in clinical trials.
 - Radiation therapy
 - Immunotherapy
- Treatment for ovarian epithelial, fallopian tube, and primary peritoneal cancer may cause side effects.
- Patients may want to think about taking part in a clinical trial.
- Patients can enter clinical trials before, during, or after starting their cancer treatment.
- Follow-up tests may be needed.

THERE ARE DIFFERENT TYPES OF TREATMENT FOR PATIENTS WITH OVARIAN EPITHELIAL CANCER.

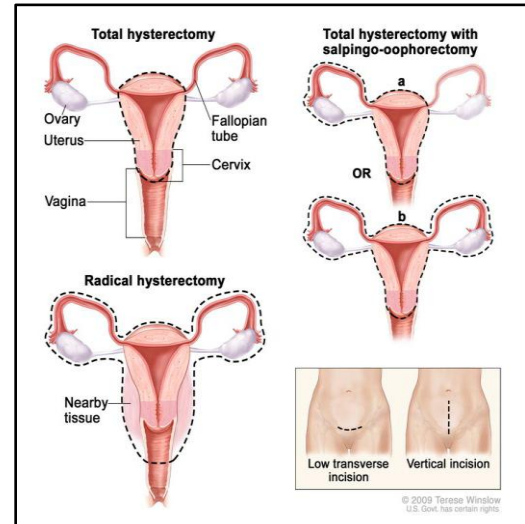
Different types of treatment are available for patients with ovarian epithelial cancer. Some treatments are standard, and some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the treatment currently used as standard treatment, the new treatment may become the standard treatment. Patients with any stage of ovarian cancer may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment.

THREE KINDS OF STANDARD TREATMENT ARE USED.

SURGERY

Most patients have surgery to remove as much of the tumor as possible. Different types of surgery may include:

- **Hysterectomy:** Surgery to remove the uterus and, sometimes, the cervix. When only the uterus is removed, it is called a partial hysterectomy. When both the uterus and the cervix are removed, it is called a total hysterectomy. If the uterus and cervix are taken out through the vagina, the operation is called a vaginal hysterectomy. If the uterus and cervix are taken out through a large incision (cut) in the abdomen, the operation is called a total abdominal hysterectomy. If the uterus and cervix are taken out through a small incision (cut) in the abdomen using a laparoscope, the operation is called a total laparoscopic hysterectomy. **ENLARG**



Hysterectomy. The uterus is surgically removed with or without other organs or tissues. In a total hysterectomy, the uterus and cervix are removed. In a total hysterectomy with salpingo-oophorectomy, (a) the uterus plus one (unilateral) ovary and fallopian tube are removed; or (b) the uterus plus both (bilateral) ovaries and fallopian tubes are removed. In a radical hysterectomy, the uterus, cervix, both ovaries, both fallopian tubes, and nearby tissue are removed. These procedures are done using a low transverse incision or a vertical incision.

- **Unilateral salpingo-oophorectomy:** A surgical procedure to remove one ovary and one fallopian tube.
- **Bilateral salpingo-oophorectomy:** A surgical procedure to remove both ovaries and both fallopian tubes.
- **Omentectomy:** A surgical procedure to remove the omentum (tissue in the peritoneum that contains blood vessels, nerves, lymph vessels, and lymph nodes).
- **Lymph node biopsy:** The removal of all or part of a lymph node. A pathologist views the lymph node tissue under a microscope to check for cancer cells.

CHEMOTHERAPY

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or

by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).

A type of regional chemotherapy used to treat ovarian cancer is intraperitoneal (IP) chemotherapy. In IP chemotherapy, the anticancer drugs are carried directly into the peritoneal cavity (the space that contains the abdominal organs) through a thin tube.

Hyperthermic intraperitoneal chemotherapy (HIPEC) is a treatment used during surgery that is being studied for ovarian cancer. After the surgeon has removed as much tumor tissue as possible, warmed chemotherapy is sent directly into the peritoneal cavity.

Treatment with more than one anticancer drug is called combination chemotherapy.

The way the chemotherapy is given depends on the type and stage of the cancer being treated.

TARGETED THERAPY

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells.

Monoclonal antibodies are immune system proteins made in the laboratory to treat many diseases, including cancer. As a cancer treatment, these antibodies can attach to a specific target on cancer cells or other cells that may help cancer cells grow. The antibodies are able to then kill the cancer cells, block their growth, or keep them from spreading. Monoclonal antibodies are given by infusion. They may be used alone or to carry drugs, toxins, or radioactive material directly to cancer cells. Monoclonal antibodies may be used in combination with chemotherapy as adjuvant therapy.

Bevacizumab is a monoclonal antibody and angiogenesis inhibitor that may be used with chemotherapy to treat ovarian epithelial cancer, fallopian tube cancer, or primary peritoneal cancer that has recurred (come back). It binds to a protein called vascular endothelial growth factor (VEGF) and may prevent the growth of new blood vessels that tumors need to grow. Other angiogenesis inhibitors are being studied in the treatment of advanced or recurrent ovarian cancer.

Poly (ADP-ribose) polymerase inhibitors (PARP inhibitors) are targeted therapy drugs that block DNA repair and may cause cancer cells to die. Olaparib, rucaparib, and niraparib are PARP inhibitors that may be used as maintenance therapy to treat certain types of ovarian epithelial cancer, fallopian tube cancer, or primary peritoneal cancer that have recurred. Veliparib is a PARP inhibitor that is being studied in combination with chemotherapy to treat advanced ovarian cancer.

NEW TYPES OF TREATMENT ARE BEING TESTED IN CLINICAL TRIALS.

This summary section describes treatments that are being studied in clinical trials. It may not mention every new treatment being studied. Information about clinical trials is available.

RADIATION THERAPY

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. Some women receive a treatment called intraperitoneal radiation therapy, in which radioactive liquid is put directly in the abdomen through a catheter. Intraperitoneal radiation therapy is being studied to treat advanced ovarian cancer.

IMMUNOTHERAPY

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This cancer treatment is a type of biologic therapy.

Vaccine therapy is a cancer treatment that uses a substance or group of substances to stimulate the immune system to find the tumor and kill it. Vaccine therapy is being studied to treat advanced ovarian cancer.

TREATMENT FOR OVARIAN EPITHELIAL, FALLOPIAN TUBE, AND PRIMARY PERITONEAL CANCER MAY CAUSE SIDE EFFECTS.

For information about side effects caused by treatment for cancer, see our Side Effects page.

PATIENTS MAY WANT TO THINK ABOUT TAKING PART IN A CLINICAL TRIAL.

For some patients, taking part in a clinical trial may be the best treatment choice. Clinical trials are part of the cancer research process. Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment.

Many of today's standard treatments for cancer are based on earlier clinical trials. Patients who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment.

Patients who take part in clinical trials also help improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward.

PATIENTS CAN ENTER CLINICAL TRIALS BEFORE, DURING, OR AFTER STARTING THEIR CANCER TREATMENT.

Some clinical trials only include patients who have not yet received treatment. Other trials test treatments for patients whose cancer has not gotten better. There are also clinical trials that test new ways to stop cancer from recurring (coming back) or reduce the side effects of

cancer treatment.

Clinical trials are taking place in many parts of the country. Information about clinical trials supported by NCI can be found on NCI's clinical trials search webpage. Clinical trials supported by other organizations can be found on the ClinicalTrials.gov website.

CONCLUSION

Ovarian cancer is the second most common gynecologic malignancy, with an estimated 22,280 new cases in 2012. An estimated 15,500 deaths were attributed to ovarian cancer in 2012, making it the deadliest gynecologic malignancy.¹ Despite improvements in the treatment of ovarian cancer, mortality has remained largely unchanged over the last 40 years.² Ovarian cancer has been called the "silent killer" because the symptoms are vague and nonspecific, leading to delayed diagnosis. While the prognosis is good for early-stage disease, approximately 60% of patients present with metastatic disease.²

Surgery and platinum-based chemotherapy are the primary treatment modalities for ovarian cancer. This review focuses on the management of epithelial ovarian cancer, which constitutes more than 80% of ovarian cancers.³ Current standards of care and the use of intraperitoneal (IP) chemotherapy will be discussed, and a brief overview of new agents being studied for their utility in improving treatment outcomes will be presented.

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