

What is
Ovarian Cancer?

Let us answer some
of your questions.

Ovarian cancer

An ESMO guide for patients

Patient information based on ESMO Clinical Practice Guidelines

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand ovarian cancer and its treatment. It contains information on the most common type of this cancer – epithelial ovarian cancer – including the causes of the disease and how it is diagnosed, up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

The medical information described in this document is based on the ESMO Clinical Practice Guideline for epithelial ovarian cancer, which is designed to help clinicians with the diagnosis and management of newly diagnosed or relapsed epithelial ovarian cancer. All ESMO Clinical Practice Guidelines are prepared and reviewed by leading experts using evidence gained from the latest clinical trials, research and expert opinion.

The information included in this guide is not intended as a replacement for your doctor's advice. Your doctor knows your full medical history and will help guide you regarding the best treatment for you.

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Ovarian cancer: A summary of key information

Introduction to ovarian cancer

- Ovarian cancer arises from cells in the **ovaries** or **fallopian tubes** that have grown abnormally and multiplied to form a lump or **tumour**.
- Epithelial ovarian cancer is a type of ovarian cancer which is differentiated from non-epithelial ovarian cancer because of the way the tumour cells look under a microscope – which in turn reflects the type of tissue from which the cancer originated. The four main types of epithelial ovarian cancer are **serous carcinoma**, **mucinous**, **endometrioid** and **clear-cell cancers**. They are diagnosed in the same way but may be treated differently.
- Ovarian cancer is the seventh most common cancer in women worldwide and predominantly affects older, postmenopausal women over 50.

Diagnosis of epithelial ovarian cancer

- A woman is most likely to be diagnosed with advanced epithelial ovarian cancer because early disease typically has no symptoms; she may have noticed bloating and abdominal discomfort or in some cases, she may become aware of swollen **lymph nodes** in her groin, armpits or in her neck just above her collarbone.
- A definitive diagnosis is possible only after surgery but initial investigations begin with a physical examination, abdominal **ultrasound scan** and blood tests, followed by a **computed tomography (CT) scan** to plan surgery.

Treatment options for epithelial ovarian cancer

- Surgery is the cornerstone of epithelial ovarian cancer management in its early stages.
- Advanced or high-risk epithelial ovarian cancer is treated predominantly with surgery and **chemotherapy** although **targeted treatments** are used in specific cases.
 - **Chemotherapy** – the use of anti-cancer drugs to destroy cancer cells. **Chemotherapy** can be given alone or with other treatments.
 - **Targeted therapy** – newer drugs that work by blocking the signals that tell cancer cells to grow.
- Ovarian cancer is 'staged' according to **tumour** size, involvement of **lymph nodes** and whether it has spread outside the abdominal cavity to other parts of the body. This information is used to help decide the best treatment.

Early-stage epithelial ovarian cancer

- Women with Stage I disease who are considered to be at intermediate or high risk of their cancer recurring will quite often be given **chemotherapy** after their surgery.

Locally advanced and metastatic epithelial ovarian cancer

- All women whose epithelial ovarian cancer has been classed as Stages II, III or IV should receive **chemotherapy** after surgery; the standard treatment is with a regimen of two drugs – **paclitaxel** and **carboplatin**.
- For women who develop an allergy to **paclitaxel** or cannot tolerate it, **docetaxel** or **pegylated liposomal doxorubicin** can be substituted and given with **carboplatin** instead.
- A targeted drug called **bevacizumab** can be added to standard **chemotherapy** with **paclitaxel** and **carboplatin** for some women who have newly diagnosed Stage III B, III C or IV epithelial ovarian cancer.

Recurrent epithelial ovarian cancer

- This will be treated with **chemotherapy**; the precise drugs and regimen used will depend on how quickly the cancer has returned and its sensitivity to treatment.
- **Bevacizumab** may be given to some women who have relapsed – in combination with a **chemotherapy doublet** or single-agent **chemotherapy** – depending on how sensitive the **tumour** was to previous treatment.
- A new type of **targeted treatment** called **olaparib** may be given if your cancer tested positive for **BRCA1** or **BRCA2 mutation** and has responded to **platinum-based chemotherapy** – this is done to help maintain the response for as long as possible.
- **Niraparib** has recently been approved for use as maintenance therapy in woman who are responding to **platinum-based chemotherapy**.

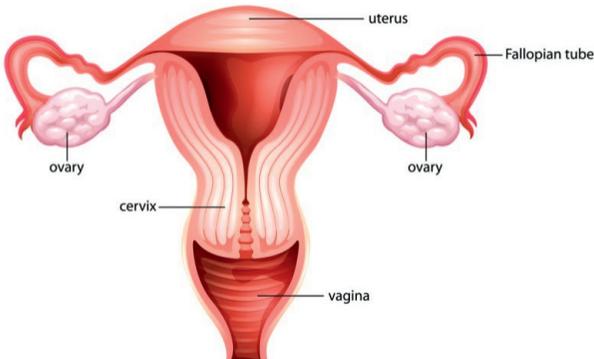
Follow-up after treatment

- You will be seen by your doctor every 3 months for the first two years after finishing treatment and then every 6 months thereafter.
- At each visit, he/she will examine you and may also do a pelvic examination, request blood tests and/or order a **CT scan** or a **positron emission tomography (PET)-CT scan** to see if your cancer has returned and how best to treat it if it has.

Anatomy of the female reproductive organs

The internal reproductive organs in a female include:

- **Vagina** (birth canal).
- **Uterus** (womb).
- **Fallopian tubes** (tubes that go to each ovary).
- **Ovaries** (small glands located either side of the **uterus** at the ends of the **fallopian tubes**).



Anatomy of the female reproductive organs, showing the **uterus**, **fallopian tubes** and **ovaries**. During her reproductive years, a woman's **ovaries** produce one mature egg every month (from either **ovary**) which is released and travels down a **fallopian tube** towards the **uterus**. If the egg is not fertilised it is shed from the body via the **vagina**, together with the lining of the **uterus**, in a process called **menstruation**. A baby girl is born with **ovaries** that contain all the eggs she will ever have – approximately 1–2 million – of which only around 500 will be released during her lifetime. The vast majority of eggs gradually die as a woman ages until eventually, any that remain are depleted at **menopause**.

What is ovarian cancer?

By far the most common type of ovarian cancer is called epithelial ovarian cancer and this accounts for approximately 90% of all women diagnosed (*Ledermann et al., 2013*). Epithelial ovarian cancer starts in the ovarian epithelium – a thin layer of cells covering the **ovary** or from the **fallopian tube** epithelium. This guide will focus exclusively on epithelial ovarian cancer.

What subtypes of epithelial ovarian cancer are there?

The four main **histological subtypes** of epithelial ovarian cancer, as follows:

- **Serous carcinoma:** This is the most common subtype accounting for around 80% of advanced ovarian cancers. These cancers are further subdivided into high-**grade tumours** and low-**grade tumours**; low-**grade tumours** represent approximately 10% of **serous carcinomas**, tend to occur in younger women and carry a better **prognosis**.
- **Mucinous:** This subtype accounts for 7%–14% of all primary epithelial ovarian cancers. The **prognosis** for this subtype is very good if diagnosed at an early stage.
- **Endometrioid:** These are responsible for ovarian cancer in around 10% of women who have it and typically are low-**grade tumours** that are diagnosed early.
- **Clear-cell cancers:** Around 5% of women with ovarian cancer will have this subtype, although it varies depending on which part of the world you are from. The **prognosis** for this subtype is quite good if it's diagnosed early.



What are the symptoms?

In its early stages, epithelial ovarian cancer may have few or no symptoms making diagnosis more difficult. Symptoms are seen more commonly in advanced disease and may include:

In all stages:

- Abdominal or pelvic pain.
- Constipation.
- Diarrhoea.
- Frequent need to urinate.
- Vaginal bleeding.
- Distended abdomen.
- Feeling extremely tired.

Ovarian cancer

In advanced epithelial ovarian cancer:

- Increased abdominal girth (skirts or trousers may feel tighter).
- Bloating.
- Feeling sick.
- Loss of appetite.
- Indigestion.
- Feeling full soon after starting to eat.
- Difficulty breathing.

You should see your doctor if you experience any of these symptoms. However, it is important to remember that these symptoms are common in people who do not have epithelial ovarian cancer; they may also be caused by other conditions.

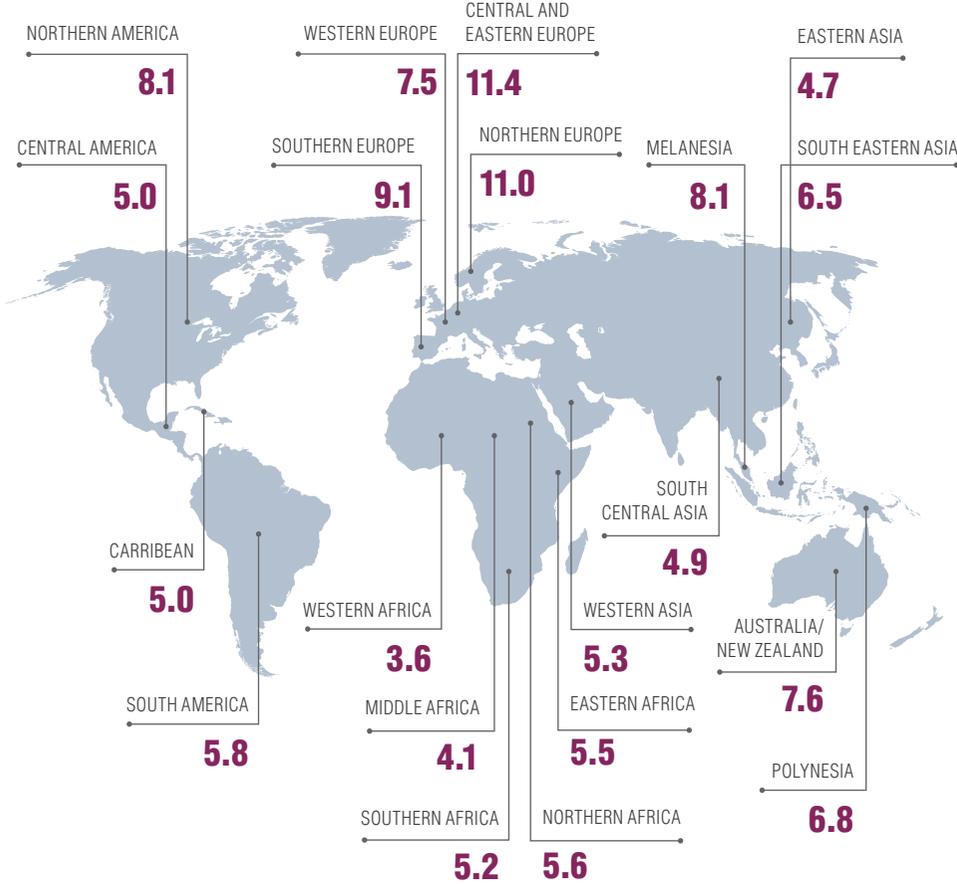
Epithelial ovarian cancer may have no symptoms in its early stages

How common is epithelial ovarian cancer?

Ovarian cancer predominantly affects older, postmenopausal women – the majority of women diagnosed are over 50. Ovarian cancer is the seventh most common cancer in women worldwide. The highest incidence of ovarian cancer is in Europe and North America and the lowest incidence in Africa and Asia (*Ferlay et al., 2013*):

Ovarian cancer is most common in women over 50

The map shows estimated numbers of new cases of ovarian cancer diagnosed in 2012 (the most recent statistics available) per 100,000 people of each region's population (*Ferlay et al., 2013*).



What causes ovarian cancer?

The precise cause of ovarian cancer is unknown, but several risk factors for developing the disease have been identified. It is important to remember that having a risk factor increases the risk of cancer developing but it does not mean that you will definitely get cancer. Likewise, not having a risk factor does not mean that you definitely won't get cancer.

FACTORS THAT INCREASE RISK	FACTORS THAT DECREASE RISK
Having more pregnancies	Oral contraceptive pill
Early onset of menstruation and late menopause	Tying-off fallopian tubes (female sterilisation)
Obesity	Breastfeeding
Family history	
BRCA1 or BRCA2 mutation	

There are various risk factors associated with developing ovarian cancer although each factor may not apply to every woman who develops the disease. Many factors that either increase or decrease the risk of developing ovarian cancer are related to a woman's reproductive history, which points to **ovulation** as being an important influence.

A woman's reproductive history is an important factor that determines her risk of developing ovarian cancer

Family history plays a very important role in whether or not a woman will develop ovarian cancer. Women with a first-degree relative with cancer are at more than twice the risk of developing ovarian cancer compared with a woman with no such family history. Women with hereditary ovarian cancer tend to develop the disease around 10 years sooner than do women with non-hereditary ovarian cancer.



BRCA mutation

Approximately 6%–25% of ovarian cancers have a **BRCA1** or **BRCA2 mutation**, with these **mutations** most frequently seen in high-**grade serous tumours** (Vergote *et al.*, 2016). Inheriting a **BRCA1 mutation** increases a woman's risk of developing ovarian cancer to 15%–45%, while inheriting a **BRCA2 mutation** increases her risk to 10%–20% (Ledermann *et al.*, 2013).

A doctor will refer a woman for **BRCA1** and **BRCA2 mutation** testing based on her family history and ethnic background. If she is found to be carrying a **mutation** in one or both of these genes, she should be given follow-up counselling during which her options for reducing the risk of developing ovarian cancer (or another type of cancer related to a **mutation** in these genes, such as breast cancer) will be discussed (Paluch-Shimon *et al.*, 2016). If a woman is still of child-bearing age, there will be implications of some risk reduction measures that she will be made aware of and needs to consider. For instance, women carrying a **BRCA1** or **BRCA2 mutation** are encouraged to have their **ovaries** and **fallopian tubes** surgically removed before they reach the age of 40 (ovarian cancer is relatively uncommon in younger women). This has obvious implications for having children.



Women who test positive for BRCA1/2 mutation will be monitored carefully and offered risk-reduction measures

Because of the early onset of ovarian cancer in women carrying a **BRCA1** or **BRCA2 mutation**, as well as the difficulties of detecting it in its early stages, women over 25 who have a family history of **BRCA1** or **BRCA2 mutation** should undergo testing or at the very least, regular monitoring (Paluch-Shimon *et al.*, 2016). Women found to have a high-**grade tumour** at surgery also should be tested for **BRCA1** and **BRCA2 mutation**.

How is epithelial ovarian cancer diagnosed?

Unless a woman is already being monitored because she has tested positive for a **BRCA1** or **BRCA2 mutation**, she is most likely to be diagnosed with advanced epithelial ovarian cancer because early disease typically has no symptoms. She may have noticed bloating and abdominal discomfort, or in some cases, she may become aware of swollen **lymph nodes** in her groin, armpits or in her neck just above her collarbone.

A diagnosis of epithelial ovarian cancer is based on the results of the following examinations and tests:

Clinical examination

Your doctor will carry out a clinical examination. He/she will examine your abdomen and check to see if any of your **lymph nodes** are enlarged. If there is a suspicion that you may have epithelial ovarian cancer, he/she may arrange for a blood test and/or abdominal **ultrasound scan**, and refer you to a specialist for further testing.

The blood test will measure a substance called **CA 125** which is raised in about 50% of women with early-stage epithelial ovarian cancer and in about 85% of those with advanced disease. **CA 125** is not specific to epithelial ovarian cancer; it can be higher than normal in people with various other types of cancer and also

in women with **non-malignant gynaecological** conditions. Because of this, it has to be considered alongside other tests before a diagnosis of epithelial ovarian cancer can be made.



Imaging

An ultrasound scan of the abdomen and pelvis is usually the first imaging investigation a doctor will do if he suspects epithelial ovarian cancer

Imaging techniques used for women in whom epithelial ovarian cancer is suspected include:

- **Ultrasound scan:** An **ultrasound scan** done with a special instrument inserted into your **vagina** gives the doctor the ability to examine your **ovaries** in terms of their size, shape and some other specific characteristics that are known to be associated with epithelial ovarian cancer.
- **Computed tomography (CT) scan:** This is a type of 'three-dimensional **x-ray**' that the specialist team can use to determine the extent of your cancer and to plan surgery if this is appropriate. It is a painless procedure that takes about 10–30 minutes.
- **Chest x-ray:** A chest **x-ray** is an alternative to a CT scan that the specialist can use to check your lungs and chest cavity for any spread of epithelial ovarian cancer.
- **Magnetic resonance imaging (MRI) scan:** Although these are not used as part of routine investigations, an **MRI scan** can be used instead of a **CT scan** to plan surgery. It uses strong magnetic fields and radio waves to produce detailed images of the inside of your body. An **MRI scanner** is a large tube, similar to a **CT scanner**, that contains powerful magnets. You lie inside the tube during the scan, which takes 15–90 minutes.



How will my treatment be determined?

Surgery is the cornerstone of management for early-stage epithelial ovarian cancer

Your treatment will depend on how far advanced your cancer is and if surgery remains an option, on surgically defined staging of your cancer (please see section below), and risk assessment. Surgery is the cornerstone of epithelial ovarian cancer management in its early stages. Surgery in all stages is best done in a specialist centre, with a highly qualified and experienced surgeon who can ensure that all traces of your cancer are removed to give you the best possible outcome (*Querleu et al., 2016*).



Establishing a treatment plan

Surgical management of early-stage epithelial ovarian cancer

The aim of surgery for early epithelial ovarian cancer is to remove the **tumour** and establish the disease stage; this will help your doctor decide if you need **chemotherapy**. Your surgeon will remove your **ovaries, fallopian tubes** and **uterus**, as well as any **lymph nodes** that may be affected. Sometimes, other tissues close to the location of the **tumour** will be removed also. This will ensure that as much of the cancer as possible is taken away along with a healthy 'margin' of tissues to help stop it coming back (*Ledermann et al., 2013*).

If you are a younger woman who has not yet completed or had a family, your surgeon may be able to offer you fertility-sparing surgery but this will depend on the precise nature of your epithelial ovarian cancer and you will be informed of any potential risks (*Morice et al., 2011*). Whatever you decide, your specialist and his/her team will support and advise you as well as carefully monitoring your health.

Surgical management of primary advanced epithelial ovarian cancer

If you have advanced epithelial ovarian cancer, it is really important for the surgeon to remove all visible traces of **tumour** as this will greatly increase your chances of a good outcome. To achieve this, he/she will do a thorough removal of all affected organs or parts of organs in your abdominal cavity. This is a big and complicated operation but one that a surgeon in a specialist centre is well qualified to perform (*Querleu et al., 2016*). All women except those in the very first stages of epithelial ovarian cancer who have low-risk disease will be given **chemotherapy** either before, or most usually, immediately after surgery (*Ledermann et al., 2013*).

Surgical management of relapsed epithelial ovarian cancer

This is not a routine intervention as clinical trials are still ongoing to evaluate its benefits.

Staging

It is important for your doctor to know the stage of the cancer so that he/she can determine the best treatment approach

Staging of the cancer is used to describe its size and position and whether it has spread from where it started. For ovarian cancers, the system used is called '**FIGO** staging' and the cancer is staged by examining tissue removed during an operation. This is known as surgical staging, and means that doctors often can't tell for sure what stage the cancer is until after surgery is done.

Cancer is staged using a sequence of letters and numbers. In the **FIGO** staging system, there are four stages designated with Roman numerals I to IV (*Prat et al., 2014*). Generally, the lower the stage the better the **prognosis**. Staging considers:

- How big the cancer is, or **tumour** size (T)
- Whether the cancer has spread to **lymph nodes** (N)
- Whether it has spread to distant sites, known as '**metastases**' (M)

For epithelial ovarian cancer, staging is done during surgery. Before surgery, imaging using **CT** or **MRI** scanning is essential to enable the surgeon to plan the operation to best effect. During surgery, **tumour** samples are taken and sent to the laboratory for **histological subtype** testing, to determine the subtype of epithelial ovarian cancer that you have.

Ovarian cancer

The different stages of ovarian cancer, including epithelial ovarian cancer, are described in the table below.

Stage I. Tumour confined to ovaries or fallopian tubes (T1-N0-M0)	IA	<ul style="list-style-type: none"> The tumour is limited to one ovary or fallopian tube and cannot be seen on the surfaces of either organ
	IB	<ul style="list-style-type: none"> The tumour is limited to both ovaries or fallopian tubes and cannot be seen on the surfaces of either organ
	IC	<ul style="list-style-type: none"> The tumour is limited to both ovaries or fallopian tubes but can be seen on the surfaces of either organ, an ovarian capsule has ruptured before surgery or free-floating tumour cells are recovered from the abdominal cavity
Stage II. Tumour involves one or both ovaries or fallopian tubes and there is evidence of cancer in other local tissues (T2-N0-M0)	IIA	<ul style="list-style-type: none"> The tumour has spread locally to the uterus
	IIB	<ul style="list-style-type: none"> The tumour has spread locally to other tissues within the abdominal cavity
Stage III Tumour involves one or both ovaries or fallopian tubes and has spread locally beyond the pelvis and/ or regional lymph nodes (T1/2-N1-M0 or T3-N0/ N1-M0)	IIIA	<ul style="list-style-type: none"> Evidence of tumour can be found in regional lymph nodes and/or it has started to spread beyond the pelvis but is not yet visible to the naked eye
	IIIB	<ul style="list-style-type: none"> There are visible metastases beyond the pelvis that measure up to 2cm across with or without evidence of tumour in regional lymph nodes
	IIIC	<ul style="list-style-type: none"> There are visible metastases beyond the pelvis that measure over 2cm across with or without evidence of tumour in regional lymph nodes
Stage IV The tumour has spread beyond the abdominal cavity to other areas of the body (any T-any N-M1)	IVA	<ul style="list-style-type: none"> Excess fluid has accumulated in the pleural cavity (the fluid-filled space that surrounds the lungs)
	IVB	<ul style="list-style-type: none"> Metastases are found in lung tissues and in other organs and lymph nodes outside the abdominal cavity

What are the treatment options for epithelial ovarian cancer?

For women whose cancer is still confined to the **ovaries** or **fallopian tubes** or has advanced only locally (Stages I or II), surgery is the primary form of treatment – with or without **chemotherapy**. Women with advanced disease may also, in certain circumstances, benefit from surgery and all will receive some form of **chemotherapy** afterwards. If your cancer relapses after treatment, it will be managed with **chemotherapy** (possibly together with **targeted therapy**) with the aim of slowing down its growth and relieving your symptoms (*Ledermann et al., 2013*).



All women except those whose epithelial ovarian cancer is in the very early stages and at low risk of spreading will be treated with chemotherapy

Adjuvant chemotherapy for early-stage disease

Women with Stage I disease who are considered to be at intermediate or high risk of their cancer recurring will quite often be given **chemotherapy** after their surgery – usually after they have had time to recover from the procedure. The treatment supported by the strongest evidence is with single-agent **carboplatin** (*Ledermann et al., 2013*).

Treatment for locally advanced and metastatic epithelial ovarian cancer

Chemotherapy

All women whose epithelial ovarian cancer has been classed as Stages II, III or IV should receive **chemotherapy** after surgery, if their cancer was operable. The standard treatment is with a regimen of two drugs – **paclitaxel** and **carboplatin** – both given **intravenously** once every three weeks (with each round of treatment called a 'cycle'). Usually, six cycles of treatment are given. For women who develop an allergy to **paclitaxel** or cannot tolerate it, **docetaxel** or **pegylated liposomal doxorubicin** can be substituted and given with **carboplatin** instead.

Targeted therapy

There is currently only one targeted drug that has been licensed in Europe for **first-line** treatment of ovarian cancer. This is called **bevacizumab** and it is a special kind of drug that stops a **tumour** from stimulating blood vessel growth and so 'starves' it of the nutrients it needs to continue growing. It is licensed in Europe in combination with **paclitaxel** and **carboplatin** for front-line treatment of women with Stage III B, III C or IV epithelial ovarian cancer (*Ledermann et al., 2013; Avastin SPC, 2017*).

Treatment for recurrent epithelial ovarian cancer

Chemotherapy

Despite the best possible treatment at diagnosis, there is still a possibility that your cancer may return. How your specialist decides to treat you will depend on many factors, including how quickly your cancer came back. Options range from sequential treatment with one **chemotherapy** drug at a time for women whose cancer has come back very quickly, a **carboplatin**-based **doublet chemotherapy** regimen if it came back more slowly, or a range of potential and mostly **platinum-based** combination options if your cancer has kept its sensitivity to **platinum**-type drugs (such as **carboplatin**). Your specialist or a member of his/her team will be happy to discuss these options with you and to explain their recommendations.

Targeted therapy

Bevacizumab also has been licensed in Europe for treating women with relapsed epithelial ovarian cancer, as follows (*Avastin SPC, 2017*):

- In combination either with **carboplatin** and **gemcitabine** or **carboplatin** and **paclitaxel** for women with a first recurrence of **platinum**-sensitive epithelial ovarian cancer who have not received previous treatment with **bevacizumab** or another agent that acts in a similar way.
- In combination with **paclitaxel**, **topotecan** or **pegylated liposomal doxorubicin** for women with **platinum**-resistant recurrent epithelial ovarian cancer who have received no more than two prior **chemotherapy** regimens and who have not received previous treatment with **bevacizumab** or another agent that acts in a similar way.

Another targeted drug that acts in a different way from **bevacizumab** is **olaparib**, which inhibits an enzyme called **PARP** that a **tumour** needs to repair its **DNA** and continue growing. **Olaparib** has been licensed in Europe as a single-agent for **maintenance treatment** of women with **platinum**-sensitive, relapsed, high-**grade, serous** epithelial ovarian cancer that has tested positive for **BRCA1 mutation** or **BRCA 2 mutation**, who have responded completely or partially to **platinum-based chemotherapy**. If you fulfil these criteria, you may be offered treatment with **olaparib** to help maintain the response to **chemotherapy** for as long as possible. Unlike many other drugs used to treat epithelial ovarian cancer, **olaparib** comes in capsule form and is taken by mouth (*Lynparza SPC, 2014*).

Niraparib is another drug that inhibits the **PARP** enzyme. In Europe, it has recently been recommended for use as **maintenance treatment** in adult woman with **platinum**-sensitive, relapsed, high-**grade, serous** epithelial ovarian, **fallopian tube**, or primary **peritoneal cancer** who are responding to **platinum-based chemotherapy**, irrespective of **BRCA1/2 mutation** status. Like **olaparib**, **niraparib** also comes in capsule form and is taken by mouth.

What are the possible side effects of treatment?

As with any medical treatment, you may experience side effects from your anti-cancer treatment. The most common side effects for each type of treatment are highlighted below, along with some information on how they can be managed. You may experience side effects other than those discussed here. It is important to talk to your doctor or **nurse specialist** about any potential side effects that are worrying you.

Fatigue is very common in patients undergoing cancer treatment, and can result from either the cancer itself or the treatments. Your doctor or nurse can provide you with strategies to limit the impact of fatigue, including getting enough sleep, eating healthily and staying active (*Cancer.Net, 2016*).



It is important to talk to your doctor about any treatment-related side effects that you are concerned about

Chemotherapy

Side effects from **chemotherapy** vary depending upon the drugs and the doses used – you may get some of those listed below but you are very unlikely to get all of them. Patients who receive a combination of different **chemotherapy** drugs are likely to experience more side effects than those who receive a single **chemotherapy** drug. The main areas of the body affected by **chemotherapy** are those where new cells are being quickly made and replaced (**bone marrow, hair follicles**, the digestive system, the lining of your mouth). Reductions in your levels of **neutrophils** (a type of white blood cell) can lead to **neutropenia**, which will make you more susceptible to infections. Some **chemotherapy** drugs can affect fertility – if you are worried about this, speak to your doctor before treatment starts. Most side effects of **chemotherapy** are temporary and can be controlled with drugs or lifestyle changes – your doctor or nurse will help you to manage them (*Macmillan, 2016a*).

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Carboplatin (Macmillan, 2015)	<ul style="list-style-type: none"> • Anaemia • Constipation • Fatigue • Hepatic (liver) toxicity • Increased risk of infection • Nausea • Neutropenia • Renal (kidney) toxicity • Thrombocytopenia • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, anaemia or thrombocytopenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Your doctor will be able to help you prevent or manage any nausea, vomiting or constipation. • You will have tests before and during treatment to check how well your kidneys and liver are functioning, and you will be asked to drink plenty of fluids to prevent your kidneys from becoming damaged.
Paclitaxel	<ul style="list-style-type: none"> • Alopecia • Anorexia • Anaemia • Arthralgia • Asthenia • Constipation • Diarrhoea • Fatigue • Fever • Leukopenia • Lymphopenia • Myalgia • Nausea • Neutropenia • Peripheral neuropathy • Rash • Stomatitis • Thrombocytopenia • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, anaemia, leukopenia, thrombocytopenia or lymphopenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. Report any fever to your doctor, as this may be a sign of infection. • Effects on the gastrointestinal system (nausea, vomiting, diarrhoea, constipation, stomatitis) may result in loss of appetite (anorexia) or feelings of fatigue/asthenia. Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience arthralgia, myalgia or rash and they will help you to manage these side effects. • Report any signs of peripheral neuropathy (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • Alopecia can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect.

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Docetaxel (Taxotere SPC, 2005)	<ul style="list-style-type: none"> • Alopecia • Anaemia • Anorexia • Asthenia • Diarrhoea • Increased risk of infections • Nausea • Neutropenia • Oedema • Peripheral neuropathy • Skin reaction • Stomatitis • Thrombocytopenia • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, anaemia or thrombocytopenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of peripheral neuropathy (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • Effects on the gastrointestinal system (nausea, vomiting, diarrhoea) and stomatitis may result in loss of appetite (anorexia) or feelings of weakness (asthenia). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience any skin reactions or fluid retention/swelling (oedema) – they will help you to manage these side effects. • Alopecia can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect.
Pegylated liposomal doxorubicin (Caelyx SPC, 2016)	<ul style="list-style-type: none"> • Hand-foot syndrome • Neutropenia • Stomatitis • Thrombocytopenia 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia or thrombocytopenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • To prevent and treat hand-foot syndrome you can try keeping hands and feet cool by exposing them to cool water (soaks, baths, or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves, or shoes that are tight fitting). • Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome or stomatitis but in most cases symptoms will be mild and will subside once you have finished treatment.

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
<p>Gemcitabine (Macmillan, 2016b)</p>	<ul style="list-style-type: none"> • Alopecia • Anaemia • Anorexia • Dry skin/rash • Dyspnoea • Fatigue • Hepatic (liver) toxicity • Increased risk of infections • Nausea • Neutropenia • Oedema • Renal (kidney) toxicity • Thrombocytopenia 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, anaemia or thrombocytopenia – your doctor may adjust your treatment according to test results, and you may need a blood transfusion if you become very anaemic. • Your doctor will prescribe anti-sickness drugs to help prevent or control sickness; if you still feel sick or are vomiting, contact the hospital as soon as possible so they can give you advice and change the anti-sickness drug to one that works better for you. • If you lose your appetite (anorexia), try to eat small meals regularly; if your appetite doesn't improve your nurse or dietitian can give you advice on getting more calories and protein in your diet. • If your ankles and legs swell (oedema), it can help to put your legs up on a foot stool or cushion; the swelling will get better after your treatment ends. • Hair loss (alopecia) is almost always temporary and your hair will grow back after chemotherapy ends; it is important to cover your head to protect your scalp when you are out in the sun. • If you have fatigue, try to pace yourself and get as much rest as you need and balance this with some gentle exercise, such as short walks.
<p>Topotecan (Hycamtin SPC, 2017)</p>	<ul style="list-style-type: none"> • Abdominal pain • Alopecia • Anaemia • Anorexia • Asthenia • Constipation • Diarrhoea • Fatigue • Fever • Infection • Leukopenia • Mucositis • Nausea • Neutropenia • Thrombocytopenia • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, anaemia or thrombocytopenia – your doctor may adjust your treatment according to test results, and you may need a blood transfusion if you become very anaemic. • Your nurse may give you injections of a drug called GCSF under the skin. It encourages the bone marrow (where blood cells are made) to make more white blood cells. • If your diarrhoea is severe, your doctor will prescribe medicine to help so make sure that you tell him/her about your symptoms. • Drinking at least two litres (three and a half pints) of fluids every day will help with constipation; try to eat more foods that contain fibre such as fruit, vegetables and wholemeal bread. • Scalp cooling is a way of lowering the temperature of the scalp to help reduce hair loss; your nurse can tell you if this is an option for you.

Very common side effects with chemotherapy (used as single drugs) in the treatment of epithelial ovarian cancer. The most recent Summary of Product Characteristics (SPCs) for individual drugs can be located at: <http://www.ema.europa.eu/ema/>.

Targeted therapies

Many common side effects in patients treated with **targeted therapies** are similar to side effects from **chemotherapy** and include effects on the **gastrointestinal system** (e.g. diarrhoea, vomiting, nausea), **bone marrow** (e.g. **neutropenia**, **anaemia**, **thrombocytopenia**) or more general effects like fatigue, but there can also be some more unusual side effects such as skin problems (e.g. rash, dry skin, nail changes, discolouration) and **hypertension** (high blood pressure). Many of the side effects from **targeted therapies** can be prevented or managed effectively. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking a **targeted therapy**.

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Bevacizumab (Avastin SPC, 2017)	<ul style="list-style-type: none"> • Anorexia • Arthralgia • Bleeding disorders • Constipation • Diarrhoea • Dysarthria • Dysgeusia • Dyspnoea • Fatigue • Headache • Hypertension • Leukopenia • Nausea • Neutropenia • Peripheral neuropathy • Rhinitis • Skin reactions • Stomatitis • Thrombocytopenia • Wound healing complications • Vomiting • Watery eyes 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, leukopenia or thrombocytopenia – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of peripheral neuropathy (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • Any treatment will be delayed until wounds have healed satisfactorily. • Your blood pressure will be monitored throughout treatment and any hypertension will be managed appropriately. • Effects on the gastrointestinal system (stomatitis, constipation, diarrhoea, nausea, vomiting) and dysgeusia (taste changes) may result in loss of appetite (anorexia). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop any skin reactions (e.g. rash, dry skin, discolouration) – they will help you to manage these side effects. • Report any other side effects, including changes in vision, dyspnoea (breathlessness), dysarthria (difficulty with speech), arthralgia (painful joints) or headache to your doctor, who will help you to manage these side effects.

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
<p>Olaparib (Lynparza SPC, 2014)</p>	<ul style="list-style-type: none"> • Anaemia • Anorexia • Diarrhoea • Dizziness • Dysgeusia • Dyspepsia • Fatigue/asthenia • Headache • Nausea • Neutropenia • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia or anaemia – your doctor may adjust your treatment according to test results, and you may need a blood transfusion if you become very anaemic. • Anti-sickness injections and tablets can control nausea and vomiting so make sure your nurse or doctor knows if you have these symptoms. • If you develop diarrhoea, drink plenty of fluids (at least 2.5 litres a day); ask your nurse about soothing creams to apply around your back passage as the skin in that area can get very sore and even break if you have severe diarrhoea. • If you have any other side effects speak to your nurse or doctor as they can help and advise you.
<p>Niraparib (Zejula PI, 2017)</p>	<ul style="list-style-type: none"> • Abdominal pain • Anaemia • Arthralgia • Back pain • Constipation • Cough • Decreased appetite • Diarrhoea • Dizziness • Dysgeusia • Dyspepsia • Dyspnoea • Fatigue/asthenia • Headache • Hypertension • Insomnia • Nasopharyngitis • Nausea • Neutropenia • Palpitations • Thrombocytopenia • Urinary tract infection • Vomiting 	<ul style="list-style-type: none"> • Your blood cell counts will be monitored frequently throughout your treatment in order to detect any neutropenia, thrombocytopenia or anaemia. • Your doctor may adjust your dose, temporarily stop or permanently stop treatment if you experience certain side effects. • Anti-sickness injections and tablets can control nausea and vomiting so make sure your nurse or doctor knows if you have these symptoms. • If you develop diarrhoea, drink plenty of fluids (at least 2.5 litres a day); ask your nurse about soothing creams to apply around your back passage as the skin in that area can get very sore and even break if you have severe diarrhoea. • Report any other side effects to your nurse or doctor, who will help you to manage these side effects.

Very common side effects with targeted therapies in the treatment of epithelial ovarian cancer. The most recent Summary of Product Characteristics (SPCs) for individual drugs can be located at: <http://www.ema.europa.eu/ema/>.

What happens after my treatment has finished?

Follow-up appointments

You will be able to discuss any concerns you have at your follow-up appointments

After your treatment has finished, your doctor will arrange follow-up appointments. During these appointments, you will typically have a clinical examination, a **CT scan**, and a blood test to measure levels of a substance called **CA 125**. In certain cases (usually when initial assessments are conflicting or unclear), a special scan called a **positron emission tomography (PET)-CT scan** may be also be used. Based on your results, your doctor will let you know how often you need to return for further follow-up appointments.



What if I need more treatment?

Cancer that comes back is called a recurrence. The treatment that you will be offered depends on the extent of the recurrence. When the **tumour** comes back as a recurrence at a single site, you may be offered further surgery followed by **chemotherapy**. Recurrent **tumours** are normally regarded as **metastatic** cancers and you can usually have further **chemotherapy**, and this may include different drugs to those you were treated with when you were first diagnosed. Sometimes, **targeted therapy** drugs are given with **chemotherapy** (see section 'Treatment for locally advanced and metastatic epithelial ovarian cancer' for more information).

Looking after your health

After you have had treatment for epithelial ovarian cancer, you may feel very tired and emotional. It is important to take good care of yourself and get the support that you need.

- **Take plenty of rest when you need it:** Give your body time to recover and make sure you rest as much as you can. Complementary therapies, such as aromatherapy, may help you relax and cope better with side effects. Your hospital may offer complementary therapy; ask your doctor for details.
- **Eat well and keep active:** Eating a healthy diet and keeping active can help improve your fitness. It is important to start slowly, with gentle walking, and build up as you start to feel better.

For further information and advice regarding how to regain your life as far as possible after treatment for cancer, see ESMO's patient guide on survivorship (<http://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship>).

Emotional support

It is common to be overwhelmed by your feelings when you have been diagnosed with cancer and when you have been through treatment. If you feel anxious or depressed, talk to your doctor or nurse – they can refer you to a specialist counsellor or psychologist who has experience of dealing with emotional problems of people dealing with cancer. It may also help to join a support group so that you can talk to other people who understand exactly what you are going through.



Support groups

In Europe, there are some ovarian cancer patient advocacy groups, which help patients and their families to navigate the epithelial ovarian cancer landscape. They can be local, national or international, and they work to ensure patients receive appropriate and timely care and education. These groups can provide you with the tools you may need to help you better understand your disease, and to learn how to cope with it, living the best quality of life that you can.

The European Network of Gynaecological Cancer Advocacy Group is a network of European patient advocacy groups (ENGAGE) that was established in 2012 to help provide information and support to patients affected by gynaecological cancers, including epithelial ovarian cancer.

For further information about ENGAGE, and to find details of patient advocacy groups in your area, visit: <http://engage.esgo.org/en/engage-map>



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GLOSSARY

ALOPECIA

Hair loss

ANAEMIA

A condition characterised by the shortage of red blood cells or haemoglobin (a protein in red blood cells that carries oxygen throughout the body)

ANOREXIA

A lack or loss of appetite

ARTHRALGIA

Pain in a joint(s)

ASTHENIA

Abnormal feeling of weakness or lack of energy

BENIGN

Not cancerous

BEVACIZUMAB

A type of **targeted therapy** used to treat some cancers, including advanced epithelial ovarian cancer. It is a monoclonal antibody that targets vascular endothelial growth factor and prevents the cancer cells from developing their own blood supply, thus helping to slow down **tumour** growth

BONE MARROW

A spongy tissue found inside some bones (e.g. hip and thigh bones). It contains stem cells, which are cells that can develop into the red blood cells, white blood cells or **platelets**

BORDERLINE

An epithelial ovarian **tumour** subtype of low **malignant** potential

BRCA1

A **gene** that normally controls **tumour** growth but when mutated has the opposite effect

BRCA2

A **gene** that normally controls **tumour** growth but when mutated has the opposite effect

CA 125

A substance that may be found in high amounts in the blood of patients with certain types of cancer, including ovarian cancer

CARBOPLATIN

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

CHEMOTHERAPY

A type of cancer treatment using medicine that kills the cancer cells by damaging them, so that they cannot reproduce and spread

CLEAR-CELL CANCERS

A subtype of epithelial ovarian cancer

CONTRACEPTIVE

An intervention to prevent pregnancy, e.g. **contraceptive pill**

COMPUTED TOMOGRAPHY (CT) SCAN

A scan using **x-rays** and a computer to create detailed images of the inside of your body

DNA

Deoxyribose nucleic acid, the chemical that carries genetic information in the cells of your body

DOCETAXEL

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

DOUBLET CHEMOTHERAPY

A combination of two different types of **chemotherapy** administered at the same time

DYSARTHRIA

Difficult or unclear articulation of speech (e.g. slurred, nasal-sounding, hoarse or excessively loud or quiet)

DYSGUESIA

A change in the sense of taste

DYSPEPSIA

The medical term for indigestion

DYSPNOEA

Shortness of breath

ENDOMETRIOID

A subtype of epithelial ovarian cancer

FALLOPIAN TUBES

A pair of tubes along which eggs travel from the **ovaries** to the **uterus** in women and other mammals

FIGO

Fédération Internationale de Gynécologie et d'Obstétrique (The International Federation of Gynecology and Obstetrics)

FIRST-LINE (TREATMENT)

The initial treatment given to a patient

GLOSSARY

GASTROINTESTINAL SYSTEM

The system of organs responsible for getting food into and out of the body and for making use of food to keep the body healthy – includes the **oesophagus**, stomach and intestines

GEMCITABINE

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

GENE

Genes are pieces of **DNA** responsible for making substances that your body needs to function

GRADE

Cancer **grade** is based on how different **tumour** cells look from normal cells under a microscope, and on how quickly they grow. The **grade** will be a value between one and three and reflects the aggressiveness of **tumour** cells; the higher the **grade**, the more aggressive the **tumour**

GYNAECOLOGICAL

A branch of medicine that deals with functions and diseases specific to women and girls, especially those affecting the reproductive system

HAIR FOLLICLE

A small sac in the skin from which hair grows from

HAND-FOOT SYNDROME

A condition marked by pain, swelling, numbness, tingling or redness of the hands or feet. It sometimes occurs as a side effect of certain anticancer drugs

HEPATIC

Relating to the liver

HISTOLOGICAL SUBTYPE

Cancer type based on the type of tissue in which the cancer started

HYPERTENSION

Abnormally high blood pressure

INTRAVENOUSLY

Administered into a vein

LEUKOPENIA

A decrease in the number of leukocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

LYMPH NODES

Small structures throughout the **lymphatic system** that work as filters for harmful substances, such as cancer cells or bacteria

LYMPHOPENIA

An abnormally low level of lymphocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

MAINTENANCE TREATMENT

Treatment given after the initial cycles of **chemotherapy** with the aim of keeping the cancer under control

MALIGNANT

Malignant means cancerous. **Malignant** cells can invade nearby tissue and spread to other parts of the body

MENOPAUSE

The **menopause** is when a woman stops having periods and is no longer able to get pregnant naturally

MENSTRUATION

This is also known as a period or monthly, and is the regular discharge (usually monthly) of blood and tissue from the inner lining of the **uterus** through the **vagina**

METASTASES

Cancerous **tumours** that have originated from a primary **tumour**/growth in another part of the body

MRI SCAN

A type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body

MUCINOUS

A subtype of epithelial ovarian cancer

MUCOSITIS

Inflammation and ulceration of the membranes lining the **gastrointestinal system**

MUTATION

A permanent alteration in the **DNA** sequence that makes up a **gene**, such that the sequence differs from what is found in most people

MYALGIA

Pain in a muscle(s)

NEUTROPENIA

An abnormally low level of **neutrophils** in the blood, which increases risk of infection

NEUTROPHILS

A type of white blood cell that play an important role in fighting off infection

GLOSSARY

NIRAPARIB

A recently-approved drug for the treatment of recurrent ovarian cancer in women responding to **platinum-based chemotherapy**

NON-MALIGNANT

Not cancerous, also referred to as '**benign**'; some growths can resemble **tumours** but are relatively harmless

NURSE SPECIALIST

A nurse specialised in the care of patients with a certain condition (e.g. cancer)

OBESITY

Abnormal or excessive fat accumulation that may impair health

OEDEMA

A build-up of fluid in the body which causes the affected tissue to become swollen

OLAPARIB

A drug used to treat advanced ovarian cancer caused by mutations (changes) in the **BRCA1** and **BRCA2 genes**

OVARIAN CAPSULE

A thin layer of tissue surrounding the **ovary**

OVARIES

A female reproductive organ in which eggs are produced and plural of the term 'ovary'

OVULATION

The process of releasing one or more eggs from the **ovaries**

PACLITAXEL

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

PARP

Poly(ADP-ribose) polymerase, an enzyme involved in repairing **DNA**

PEGYLATED LIPOSOMAL DOXORUBICIN

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

PERIPHERAL NEUROPATHY

Damage to the nerves in the extremities of the body. Symptoms may include pain, sensitivity, numbness or weakness in the hands, feet or lower legs

PERITONEAL CANCER

Cancer of the peritoneum, a membrane that forms the lining of the abdominal cavity

POSITRON EMISSION TOMOGRAPHY (PET)

An imaging test that uses a dye with radioactive tracers, which is injected into a vein in your arm

PLATINUM

A metal that is an important component of some anticancer drugs, such as **carboplatin**

PLATINUM-BASED

A combination of **chemotherapy** drugs that includes a platinum (i.e. cisplatin or **carboplatin**)

PROGNOSIS

The likely outcome of a medical condition

RENAL

Relating to the kidneys

RHINITIS

Inflammation of the lining inside the nose

SEROUS

The most common subtype of epithelial ovarian cancer

STERILISATION

Surgery to make a female unable to have children

STOMATITIS

Inflammation of the inside of the mouth

TARGETED THERAPY

A newer type of cancer treatment that uses drugs or other substances to precisely identify and attack cancer cells, usually while doing little damage to normal cells

THROMBOCYTOPENIA

A deficiency of platelets in the blood. This causes bleeding into the tissues, bruising, and slow blood clotting after injury

TOPOTECAN

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest or can be given in oral form, as capsules

TUMOUR

A lump or growth of abnormal cells. **Tumours** may be **benign** (not cancerous) or **malignant** (cancerous). In this guide, the term '**tumour**' refers to a cancerous growth, unless otherwise stated

ULTRASOUND SCAN

A type of medical scan where sound waves are converted into images by a computer

GLOSSARY

UTERUS

A hollow, pear-shaped organ that is located in a woman's lower abdomen in which a baby develops before birth; also called the womb

VAGINA

A muscular tube leading from the **uterus** to the outside of the body

X-RAY

An imaging test, using a type of radiation that can pass through the body, which allows your doctor to see images of inside your body

This guide has been prepared to help you, your friends and your family better understand the nature of epithelial ovarian cancer and the treatments that are available. The medical information described in this document is based on the clinical practice guideline of the European Society for Medical Oncology (ESMO) for the management of newly diagnosed and relapsed epithelial ovarian cancer. We recommend that you ask your doctor about the tests and types of treatments available in your country for your type and stage of epithelial ovarian cancer.

This guide has been written by Kstorfin Medical Communications Ltd on behalf of ESMO.

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**We can help you understand ovarian cancer
and the available treatment options.**

The ESMO Guides for Patients are designed to assist patients, their relatives and caregivers to understand the nature of different types of cancer and evaluate the best available treatment choices. The medical information described in the Guides for Patients is based on the ESMO Clinical Practice Guidelines, which are designed to guide medical oncologists in the diagnosis, follow-up and treatment in different cancer types.

For more information, please visit www.esmo.org

