ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Cervical Cancer

What is **Cervical Cancer**?

Let us answer some of your questions.

ESMO Patient Guide Series

based on the ESMO Clinical Practice Guidelines

esmo.org

Cervical 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 cervical cancer and its treatment. It contains information on 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 cervical cancer, which is designed to help clinicians with the diagnosis and management of cervical 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.

Words highlighted in **colour** are defined in the glossary at the end of the document.

This guide has been developed and reviewed by:

Representatives of the European Society for Medical Oncology (ESMO):
Nicoletta Colombo; Claire Bramley; Francesca Longo; Jean-Yves Douillard; and Svetlana Jezdic

Representatives of the European Oncology Nursing Society (EONS):
Anita Margulies; Lise Bjerrum Thisted

Patient advocate: Maria Holtet Rüsz

WHAT'S INSIDE

Cervical cancer: A summary of key information

Introduction to cervical cancer

- Cervical cancer forms in the tissues of the **cervix** and is almost always caused by **human papillomavirus** (**HPV**) infection.
- **HPV** vaccines are available that provide protection against **HPV** infection and decrease the incidence of high-grade cervical abnormalities.
- In its early stages, cervical cancer often has no symptoms, and is most likely to be detected through cervical screening tests.
- Cervical cancer is the fourth most common cancer in women worldwide and predominantly affects women under the age of 45.

Diagnosis of cervical cancer

- Early cervical cancer typically has no symptoms. Symptoms of advanced cervical cancer include abnormal vaginal bleeding, pelvic pain, vaginal discharge and pain during sex.
- A diagnosis of cervical cancer is usually based on the results of clinical examination, **colposcopy** and **biopsy**.
- Further investigations help to determine how advanced the cancer is, e.g. examination under anaesthesia, **x-ray** and **intravenous pyelogram**. Modern imaging techniques such as **computed tomography** (**CT**), **magnetic resonance imaging** (**MRI**) and **positron emission tomography** (**PET**) **scans** may also be used.
- Cervical cancer is 'staged' according to **tumour** size, involvement of **lymph nodes** and whether it has spread to other parts of the body. This information is used to help decide the best treatment.

Treatment options for cervical cancer

- Treatment for cervical cancer depends upon the size, location and stage of the **tumour**.
- Patients should be fully informed and involved in decisions about treatment options.
- Surgery is the cornerstone of cervical cancer management in its early stages. More advanced disease may be treated with **chemoradiotherapy**, **chemotherapy**, **radiotherapy** or **targeted therapies**.

Non-invasive cervical intraepithelial neoplasia

- In non-invasive **cervical intraepithelial neoplasia** (**CIN**), cells in the **cervix** show abnormal changes that may progress to cervical cancer in the future. Some patients with **CIN** require no treatment but others will undergo a procedure (e.g. **loop electrosurgical excision** or **conisation**) to remove the area of abnormal cells.

Early-stage cervical cancer

- Women with early-stage invasive disease normally undergo surgery to remove the cancer. A **hysterectomy** is usually offered, and some pelvic **lymph nodes** may also be removed.
- Patients who are considered to be at high risk of the cancer recurring may be given **adjuvant chemoradiotherapy** after their surgery.
- **Fertility-sparing** surgery options may be available for patients who want to have children in the future (e.g. a **trachelectomy** may be performed instead of a **hysterectomy** to preserve the **uterus**).

Locally advanced cervical cancer

- Locally advanced disease is usually treated with **cisplatin**-based **chemoradiotherapy**.
- Some patients may be offered **neoadjuvant chemotherapy** to shrink the **tumour**, followed by surgery.

Metastatic cervical cancer

- Metastatic disease is typically treated with **chemotherapy** (**paclitaxel** and **cisplatin**) in combination with a newer **targeted therapy** called **bevacizumab**.
- **Palliative radiotherapy** may be used to treat certain symptoms arising from **metastases**.

Recurrent cervical cancer

- Treatment for recurrent disease depends on the extent of the **recurrence**.
- If the **tumour** comes back as a **recurrence** at a single site in the pelvis, **radiotherapy** or **pelvic exenteration** may be offered.
- Recurrent **tumours** in distant organs are regarded as metastatic cancers and may be treated with **chemotherapy** with or without **targeted therapy**.

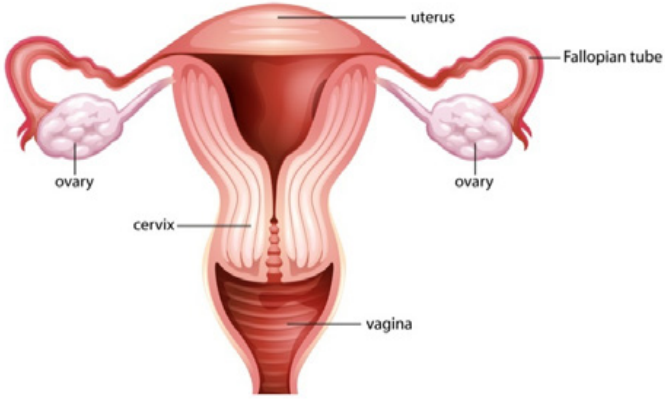
Follow-up after treatment

- The timings of follow-up appointments vary between regions and practices; you will typically be seen by your doctor every 3–6 months in the first 2 years after treatment, every 6–12 months after 3 years and annually after 5 years.
- At each visit, he/she will examine you and perform a pelvic examination. You might also have a **CT** or **PET/CT scan**.
- Support groups can help patients and their families to better understand cervical cancer, and to learn how to cope with all aspects of the disease, from diagnosis to long-term physical and emotional effects.

Anatomy of the female reproductive organs

The internal reproductive organs in a female include:

- **Cervix** (narrow end of the **uterus** that forms a canal between the **uterus** and **vagina**).
- **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 **vagina**, **uterus**, **cervix**, **fallopian tubes** and **ovaries**.*

What is cervical cancer?

Cervical cancer is a cancer that forms in the tissues of the **cervix**. It is usually a slow-growing cancer that may not have symptoms but can be detected through screening tests. Cervical cancer is almost always caused by **HPV** infection, with **HPV** detected in 99% of cervical **tumours** *(Marth et al. 2017)*.

Cervical cancer is usually a slow-growing cancer with few symptoms

What are the different types of cervical cancer?

There are three categories of cervical cancer:

- **Squamous tumours**: This is the most common subtype, accounting for 70%–80% of cervical cancers. **Squamous** cell carcinoma begins in the thin, flat cells that line the **cervix**.
- **Glandular tumours** (**adenocarcinoma**): This subtype accounts for 20%–25% of cervical cancers. **Adenocarcinoma** begins in cervical cells that make mucus and other fluids.
- **Other epithelial tumours**: These rarer subtypes include adenosquamous carcinoma, neuroendocrine **tumours** and undifferentiated carcinoma.

Cervical cancer is classified by how advanced the disease is:

Non-invasive cervical intraepithelial neoplasia

Cervical intraepithelial neoplasia (**CIN**) is a term used to describe abnormal changes to the **squamous** cells of the **cervix**. This is not cancer but may progress to cancer in the future. **CIN** is categorised into three grades:

- **CIN** 1: Up to one third of the thickness of the lining covering the **cervix** has abnormal cells.
- **CIN** 2: Between one third and two thirds of the lining covering the **cervix** has abnormal cells.
- **CIN** 3: The full thickness of the lining covering the **cervix** has abnormal cells.

The cell changes in **CIN** 1 often return to normal over time and in most patients, no treatment is needed. In patients with **CIN** 2 and **CIN** 3, treatment can be given to remove the abnormal cells to prevent them progressing to invasive cervical cancer.

Abnormal cells in the cervix may require treatment to prevent them progressing to cancer in the future

Early cervical cancer

Cervical cancer is described as early if the **tumour** has not spread beyond the **cervix**. These cancers are typically operable and the primary treatment is usually surgery to remove the cancer.

Locally advanced cervical cancer

Cervical cancer is locally advanced if it has spread outside the **cervix** into the surrounding tissues. Treatment for locally advanced cervical cancer usually starts with **chemoradiotherapy**, but in some cases, surgery may be performed if the **tumour** shrinks after **neoadjuvant** treatment.

Metastatic cervical cancer

Cervical cancer is described as metastatic when it has spread to other parts of the body, such as the lungs. **Tumours** at distant sites are called **metastases**. Metastatic cervical cancer is not curable but is treatable.

What are the symptoms of cervical cancer?

In its early stages, cervical cancer often has no symptoms. Symptoms that may be seen in advanced disease include *(Marth et al. 2017)*:

- Abnormal vaginal bleeding between menstrual periods or during/after sex or exercise.
- Pelvic pain.
- Vaginal discharge.
- Pain or discomfort during sex.

Cervical cancer often has no symptoms in its early stages

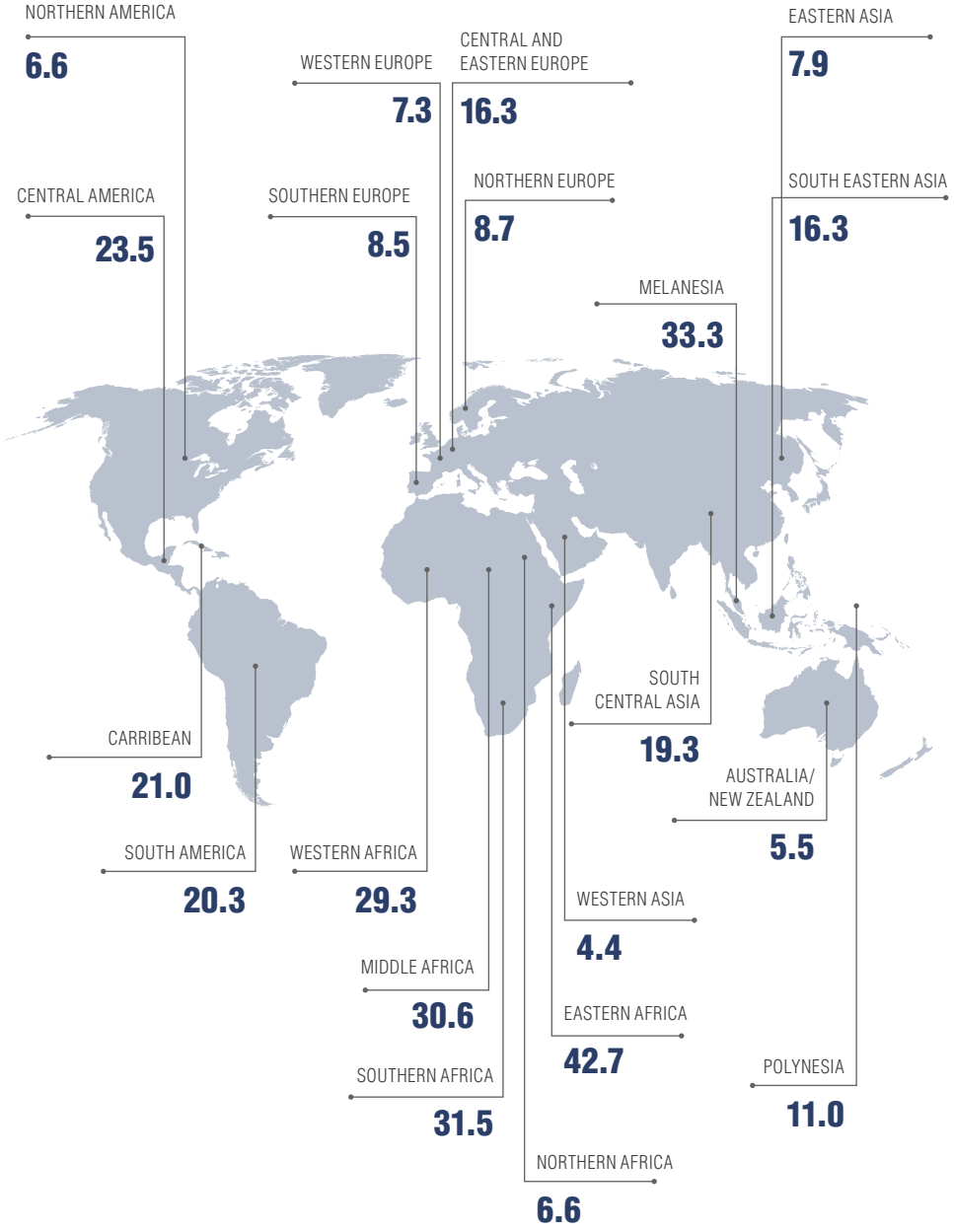
You should see your doctor if you experience any of these symptoms. However, it is important to remember that these symptoms are common in people who do not have cervical cancer; they may also be caused by other conditions.

How common is cervical cancer?

Cervical cancer is most common in younger women

Cervical cancer predominantly affects younger women – more than half of cervical cancer cases occur in women under the age of 45 years. Cervical cancer is the fourth most common cancer in women worldwide. The highest incidences of cervical cancer are reported in Eastern, Southern, Middle and Western Africa and Melanesia, and the lowest incidences are in Australia/New Zealand and Western Asia (*Ferlay et al. 2013*). Nearly 90% of cervical cancer deaths occur in developing countries and the large geographic variation in cervical cancer rates reflects differences in screening availability and **HPV** infection prevalence (*Marth et al. 2017*).

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



What causes cervical cancer?

The most significant cause of cervical cancer is persistent **HPV** infection *(Marth et al. 2017)*. **HPV** is very common and most sexually active people come into contact with the virus during their lifetime. In most people, the virus causes no harm and resolves without treatment. Although most types of **HPV** are harmless, some can cause genital warts and some can cause changes that may develop into cancers, including cervical cancer. **HPV** is detected in 99% of cervical **tumours**, particularly subtypes **HPV** 16 and **HPV** 18, which are believed to cause 70% of cervical cancer cases.

Long-term infection with a high-risk HPV is the most common cause of cervical cancer

Several other risk factors for developing cervical cancer have also 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
Persistent infection with a high-risk **HPV**	Safer sex using barrier methods to reduce the risk of **HPV** infection
HIV and AIDS	**HPV** vaccination to prevent **HPV** infection
Presence of other sexually transmitted infections alongside **HPV**	Cervical screening to detect precancerous abnormal cell changes in the **cervix**
Smoking	
Use of the contraceptive pill	
Having children	
Family history	
Previous cancer of the **vagina**, **vulva**, kidney or **urinary tract**	

There are various risk factors associated with developing cervical cancer although each factor may not apply to every woman who develops the disease.

HPV vaccination

Three **HPV** vaccines are currently available, and all three provide protection against **HPV** 16 and **HPV** 18 *(Marth et al. 2017)*. Reports from countries with established **HPV** vaccination programmes have shown that **HPV** vaccination decreases the incidence of high-grade cervical abnormalities and reduces the prevalence of the **HPV** types targeted by the vaccines. The effect of **HPV** vaccination on the incidence of cancer is not yet known but it is expected to prevent more than 70% of cervical cancers *(Marth et al. 2017)*.

Screening

Cervical screening involves taking a sample of cells from the **cervix** to check for markers of cervical cancer. Until recently, the **Papanicolaou** (**Pap**) **test**, in which cervical samples were checked for the presence of abnormalities, was the standard method for cervical cancer screening *(Marth et al. 2017)*. The **Pap test** has reduced the incidence of cervical cancer by 60%–90% and the death rate by 90%. More recently, an **HPV DNA** screening test has been introduced, which has better sensitivity for high grade **CIN** than the **Pap test** and has been shown to provide 60%–70% greater protection against invasive cancer compared with the **Pap test**.

Prevention of cervical cancer is possible via immunisation with HPV vaccines and cervical screening

How is cervical cancer diagnosed?

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

Clinical examination

If you have symptoms of cervical cancer, your doctor will carry out a clinical examination. He/she will look at your **cervix** and **vagina** to check for abnormalities. He/she may also do an internal pelvic examination, using his/her gloved fingers to check your **vagina** for lumps or changes, while pressing on your abdomen with his/her other hand. Following the clinical examination, you may need additional tests.

Colposcopy

A colposcopy is usually carried out when cervical cancer is suspected

If you have had an abnormal result from a cervical screening test, or if you have symptoms that your doctor thinks may be caused by cervical cancer, you will typically have a **colposcopy**. A **colposcopy** is a test that allows doctors to look at the **cervix** in detail, using a large magnifying glass. Samples (**biopsies**) of any abnormal areas may also be taken during a **colposcopy**. Sometimes, treatment on abnormal cells is given during the **colposcopy**. In other cases, no treatment is given until the **biopsy** results are available.

Cone biopsy

Cone **biopsies** are used to help diagnose cervical cancer and to treat abnormal cervical cells. During a cone **biopsy**, a cone-shaped piece of tissue is removed from the **cervix** under **general anaesthetic**. The sample is examined under a microscope to check for cancer cells, or to check that all abnormal cells have been removed.

How will my treatment be determined?

Your treatment will depend on the staging of your cancer and risk assessment.

Staging

Staging of the cancer is used to describe its size and position and whether it has spread from where it started. For cervical cancer, the system used is called '**FIGO** staging' and the cancer is staged by assessing **tumour** size, spread and the presence of any distant **metastases** *(Marth et al. 2017)*. Staging of cervical cancer may require several investigations, for example:

- Examination under anaesthesia: This is a detailed examination of the **cervix**, **vagina**, **uterus**, bladder and rectum under **general anaesthetic** to check for signs of cancer spread around the **cervix**. **Biopsies** are taken from any abnormal areas to check for cancer cells.
- Chest **x-ray**: A chest **x-ray** is used to check the lungs and chest cavity for any spread of cervical cancer.
- **Intravenous pyelogram:** This is an **x-ray** of the **urinary tract** taken after a special dye is injected into a vein. This test can find any abnormal areas in the **urinary tract** caused by the spread of cervical cancer.

Staging helps to determine the most appropriate treatment for cervical cancer

Other imaging techniques are also available to help with disease staging (increasingly replacing the need for chest **x-ray** and **intravenous pyelogram**) and might also be used to help determine the best treatment *(Marth et al. 2017)*:

- **Computed tomography (CT) scan**: This is a type of 'three-dimensional **x-ray**'. The **CT** scanning machine is large and shaped like a doughnut. Usually the patient lies on the machine couch on their back, and the couch slides backwards and forwards through the hole of the scanner. **CT scans** can be used to determine the extent of the cancer and may be used instead of chest **x-ray** and **intravenous pyelogram** for staging. **CT scans** can also help to detect if the cancer has spread to **lymph nodes** *(Marth et al. 2017)*.

- **Magnetic resonance imaging (MRI) scan**: **MRI scans** use strong magnetic fields and radio waves to produce detailed images of the inside of the body. An **MRI** scanner is a large tube, similar to a **CT** scanner, that contains powerful magnets. **MRI scans** can determine **tumour** size and spread with high accuracy *(Marth et al. 2017)*.

- **Positron emission tomography (PET) scan**: **PET scans** use a radioactive substance injected into a vein to show up areas of the body where cells are more active than normal. Most **PET scans** are now performed along with a **CT scan** to give detailed information about the cancer. **PET/CT scans** may be particularly useful for detecting the spread of cancer to **lymph nodes** *(Marth et al. 2017)*.

New imaging techniques are gradually replacing older methods, providing increasingly accurate information about the extent of disease

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. Generally, the lower the stage, the better the **prognosis**. The TNM system (T – **tumour**, N – nodes, M – **metastases**) is used alongside the **FIGO** system to stage cervical cancer. TNM staging considers:

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

If a **tumour biopsy** has been taken, it will be sent to the laboratory for **histological subtype** testing, to determine the subtype of cervical cancer that you have.

The different **FIGO** stages of cervical cancer are described in the table below *(Marth et al. 2017)*.

FIGO STAGE I. **Tumour** confined to the **cervix** (T1-any N-M0)	**IA**	Invasive carcinoma diagnosed only by microscopy. **Stromal invasion** with a maximal depth of 5 mm measured from the base of the epithelium and a horizontal spread of ≤7 mm • IA1: Measured **stromal invasion** ≤3 mm in depth and ≤7 mm in horizontal spread • IA2: Measured **stromal invasion** >3 mm and ≤5 mm with a horizontal spread of ≤7 mm
	IB	Clinically visible lesion confined to the **cervix** or microscopic lesion greater than IA2 • IB1: Clinically visible lesion ≤4 cm in greatest dimension • IB2: Clinically visible lesion >4 cm in greatest dimension
FIGO STAGE II. **Tumour** invades beyond **uterus** but not to pelvic wall or to lower third of **vagina** (T2-any NM0)	**IIA**	**Tumour** without **parametrial** invasion IIA1: Clinically visible lesion ≤4 cm in greatest dimension IIA2: Clinically visible lesion >4 cm in greatest dimension
	IIB	**Tumour** with **parametrial** invasion
FIGO STAGE III. **Tumour** involves lower third of beyond **vagina**, or extends to pelvic wall, or causes **hydronephrosis** or non-functioning kidney (T3-any N-M0)	**IIIA**	**Tumour** involves lower third of **vagina**
	IIIB	**Tumour** extends to pelvic wall, or causes **hydronephrosis** or non-functioning kidney
FIGO STAGE IV. **Tumour** extends beyond the true pelvis or has clinically involved the **mucosa** of the bladder and/or rectum (T4-any N-M0 or any T-any N-M1)	**IVA**	**Tumour** invades **mucosa** of the bladder or rectum, or extends beyond true pelvis
	IVB	The cancer has spread to distant organs beyond the pelvic area, such as distant **lymph nodes**, lungs, bones or liver

What are the treatment options for cervical cancer?

Your treatment will depend upon the size, location and stage of the **tumour**, as well as your general health and level of fitness. The choice of treatments will be discussed with you and your preferences will be taken into account.

It is important that patients are fully involved in the treatment decision-making – when there are several treatments available, doctors should involve patients in making decisions about their care so that the patients can choose the care that meets their needs and reflects what is important to them. This is called 'shared decision making'.

Your doctor will be happy to answer any questions you have about your treatment. Three simple questions that may be helpful when talking with your doctor or any healthcare professional involved in your care are:

- What treatment options do I have?
- What are the possible advantages and disadvantages of these options?
- How likely am I to experience these advantages and disadvantages?

It is important that patients are fully involved in discussions and decisions about their treatment

You may receive one or more of the following treatments for cervical cancer.

Surgery

The aim of surgery for cervical cancer is to remove all cancer cells. This may involve **conisation** (removal of a cone-shaped section of the **cervix**), **hysterectomy** (in which the **uterus** and **cervix** are completely removed) or a **trachelectomy** (which leaves behind the **uterus**). During surgery for cervical cancer, some **lymph nodes** in the pelvis may also be removed.

Chemoradiotherapy

Chemoradiotherapy is a combination of **chemotherapy** and **radiotherapy**. **Chemotherapy** destroys cancer cells and **radiotherapy** uses **ionising radiation** to damage the **DNA** of cancerous cells, causing them to die. **Chemoradiotherapy** for cervical cancer consists of external **radiotherapy** and/or internal **radiotherapy** (**brachytherapy**) at the same time as a course of **chemotherapy**.

Chemotherapy

Chemotherapy may be used to treat some patients with locally advanced cervical cancer, and as a **palliative** treatment in metastatic disease.

Radiotherapy

Radiotherapy is used to treat some patients with locally advanced cervical cancer (as an element of **chemoradiotherapy**) and can also be used to treat some symptoms of metastatic disease.

Targeted therapies

Targeted therapies are drugs that block specific signalling pathways in cancer cells that encourage them to grow. The **vascular endothelial growth factor** (**VEGF**) inhibitor **bevacizumab** stops **tumours** from stimulating blood vessel growth within the **tumour**, starving them of the oxygen and nutrients they need to continue growing.

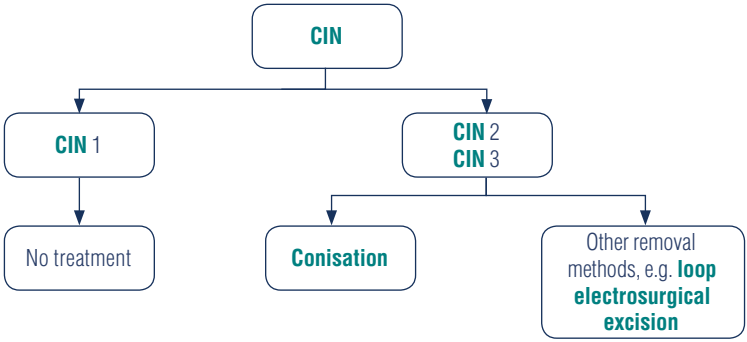
There are a number of treatments currently available to treat cervical cancer

.

What are the treatment options for CIN?

Cervical intraepithelial neoplasia (**CIN**), which is usually detected through cervical screening, is not cancer but if these abnormal cells are left untreated, there is a risk that they could develop into cervical cancer in the future. **CIN** 1 does not usually need treatment, but patients with **CIN** 2 or **CIN** 3 will typically undergo a procedure to remove the area of abnormal cells. Common procedures include **loop electrosurgical excisio**n, in which a thin loop of electrically charged wire is used to remove the abnormal tissue and seal the wound at the same time, and **conisation**, which surgically removes the abnormal cells within a cone-shaped section of **cervix** tissue.

CIN is not cancer but may need to be treated to prevent cancer developing in the future



Flowchart showing treatment approaches for CIN.

What are the treatment options for early-stage cervical cancer?

Surgery

Early disease is usually treated by surgical removal of the cancer. The aim of surgery is to remove the cancer as well as a healthy **margin** of tissue around it. After the operation, the removed tissue is examined under a microscope to check that all of the cancer was removed.

In patients with Stage IA1 cervical cancer without **lymphovascular invasion**, a simple **hysterectomy** may be offered *(Marth et al. 2017)*, in which the **cervix** and **uterus** are removed. Patients with Stage IA1 disease with **lymphovascular invasion** may also have some pelvic **lymph nodes** removed to check if the cancer has spread to them. A procedure called **sentinel lymph node dissection** (**SLND**), in which the first **lymph nodes** to which cancer cells are most likely to spread from a **tumour** are identified, removed and checked for the presence of cancer cells, may also be considered in patients with Stage I disease with **tumours** measuring ≤4 cm (Marth et al. 2017).

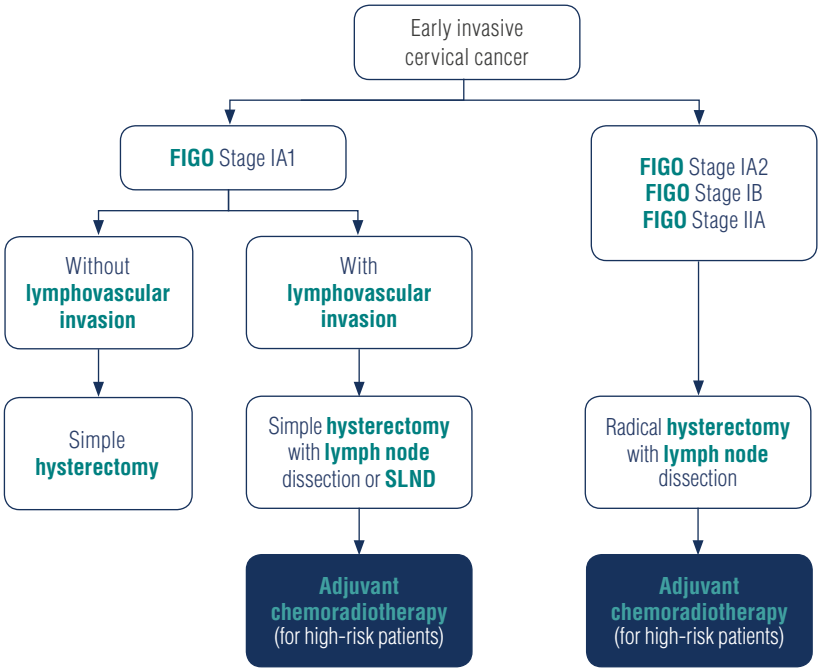
Patients with Stage IA2, IB and IIA cervical cancer typically undergo radical **hysterectomy** with **lymph node** dissection *(Marth et al. 2017)*. Radical **hysterectomy** involves the removal of the **uterus**, **cervix**, all of the surrounding tissues that hold the **uterus** in place, the upper section of the **vagina** and all of the **lymph nodes** around the **uterus**. The **ovaries** and **fallopian tubes** may also be removed.

Surgery is the cornerstone of treatment for early-stage cervical cancer

Adjuvant treatment

Following surgery to remove cervical cancer, some patients will receive **adjuvant** treatment with **chemoradiotherapy**. **Adjuvant chemoradiotherapy** is usually recommended for patients who are considered to be at a high risk of the cancer recurring – for example, if the tissue removed during surgery shows cancer cells at the surgical **margins** or in the **lymph nodes** *(Marth et al. 2017)*.

continued overleaf



Flowchart showing treatment approaches for early invasive cervical cancer.

Fertility preservation

As cervical cancer often affects women of childbearing age, **fertility-sparing** surgery is an important consideration *(Halaska et al. 2015)*. Patients who wish to preserve their fertility and have Stage IA1 cervical cancer without **lymphovascular invasion** are typically treated with **conisation** or simple **trachelectomy** *(Marth et al. 2017)*. Simple **trachelectomy** involves the removal of the **cervix** and **endocervical channel**, leaving the **uterus** intact *(Halaska et al. 2015)*. Patients with Stage IA2 disease may be treated with **conisation** or radical **trachelectomy** with pelvic **lymph node** dissection, in which most of the **cervix** and the upper part of the **vagina** is removed *(Marth et al. 2017)*. Stage IB1 cancers measuring ≤2 cm may be treated with radical **trachelectomy** with pelvic **lymph node** dissection, while Stage IB **tumours** measuring >2 cm may require pre-surgical (**neoadjuvant**) treatment with **chemotherapy** before **conisation** or **trachelectomy** *(Marth et al. 2017)*.

Fertility-sparing surgery options may be possible for patients who wish to have children in the future

It is important to understand that **fertility-sparing** surgery in early-stage cervical cancer remains an experimental approach; your doctor will fully explain the pros and cons of the available options. **Fertility-sparing** surgery is only offered to women with a strong desire for pregnancy; if your childbearing desire has been fulfilled, then standard radical surgery is considered to be the best treatment option.

What are the treatment options for locally advanced cervical cancer?

Chemoradiotherapy

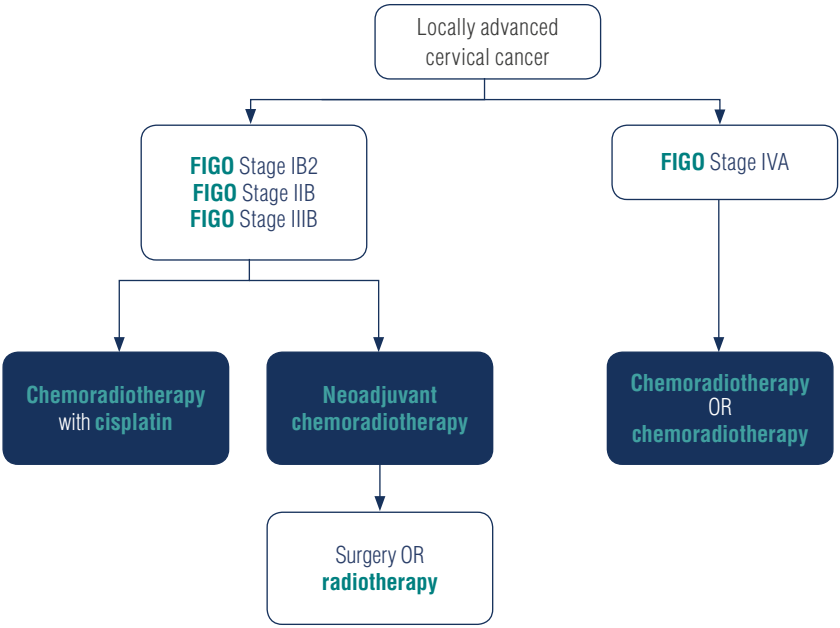
Chemoradiotherapy is the standard primary treatment for patients with locally advanced cervical cancer, with **cisplatin**-based **chemoradiotherapy** the most commonly used regimen *(Marth et al. 2017)*. Both external **radiotherapy** and **brachytherapy** may be used in this setting.

Chemoradiotherapy is the standard treatment for locally advanced disease

Neoadjuvant chemotherapy

Neoadjuvant chemotherapy may be given to certain patients with locally advanced disease to reduce the size of the **tumour** before subsequent surgical removal *(Marth et al. 2017)*. **Neoadjuvant chemotherapy** followed by **radiotherapy** may also be considered in some patients; this approach is being investigated in ongoing **clinical trials** but is not currently a common treatment strategy.

continued overleaf



Flowchart showing treatment approaches for locally advanced cervical cancer.

What are the treatment options for metastatic cervical cancer?

The aim of treatment for metastatic cervical cancer is to relieve symptoms and improve quality of life.

Metastatic cervical cancer is not curable, but is treatable

Chemotherapy

Palliative chemotherapy is typically given to patients who are able to tolerate treatment. The **chemotherapy** drugs **paclitaxel** and **cisplatin** are often used as **first-line** therapy for metastatic disease, in combination with a newer **targeted therapy** called **bevacizumab** *(Marth et al. 2017)*. Other **chemotherapy** drugs that might be used in this setting include **carboplatin** and **topotecan**.

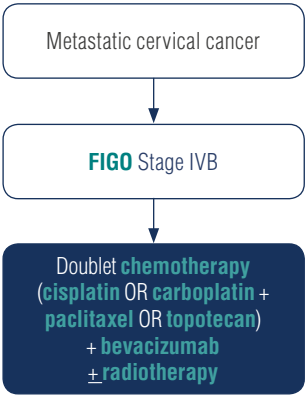
Targeted therapies

Bevacizumab, a **VEGF** inhibitor, is approved in Europe and the USA for the **first-line** treatment of metastatic or recurrent cervical cancer in combination with **paclitaxel** and **cisplatin**, or **paclitaxel** and **topotecan** in patients who are not able to tolerate **platinum-based chemotherapy** *(Avastin SPC, 2018)*.

Radiotherapy

Radiotherapy is sometimes used to treat patients with recurrent disease or certain **lymph node metastases**. It may also be used to treat the symptoms arising from **metastases** and to manage slow-growing lung **metastases** *(Marth et al. 2017)*.

continued overleaf



Flowchart showing treatment approaches for metastatic cervical cancer.

Cervical cancer and pregnancy

Cancer treatment can be harmful to unborn babies. If you are pregnant, your doctor will explain all of the potential risks to the baby, and how your pregnancy might affect your cancer treatment. Depending on the stage of your cancer, it may be possible to delay treatment until after your baby is born. Some types of **chemotherapy** may be given during pregnancy, including **platinum-based** drugs with or without **paclitaxel** *(Cordeiro and Gemignani 2017)*. Patients with Stage IA1 cervical cancer may be able to deliver their baby vaginally, but many women will have to deliver by caesarean section. Your doctor may also discuss the possibility of terminating the pregnancy. These are difficult decisions to consider but your doctor will guide you through all of your options.

Treatment for cervical cancer in pregnant women requires thorough discussion of the risks to both mother and baby

Clinical trials

Your doctor may ask you whether you would like to take part in a **clinical trial**. This is a research study conducted with patients in order to *(ClinicalTrials.gov 2017)*:

- Test new treatments.
- Look at new combinations of existing treatments or change the way they are given to make them more effective or reduce side effects.
- Compare the effectiveness of drugs used to control symptoms.
- Find out how cancer treatments work.

Clinical trials help to improve knowledge about cancer and develop new treatments and there can be many benefits to taking part. You would be carefully monitored during and after the study and the new treatment may offer benefits over existing therapies. It's important to bear in mind, however, that some new treatments are found not to be as good as existing treatments or to have side effects that outweigh the benefits *(ClinicalTrials.gov 2017)*.

Clinical trials help to improve knowledge about diseases and develop new treatments – there can be many benefits to taking part

Several new drugs for the treatment of cervical cancer are now entering **clinical trials**, including **immunotherapy** agents, which stimulate the body's immune system to fight cancer cells. **Nivolumab**, an **immunotherapy** drug which blocks a protein called **programmed cell death protein 1** (**PD-1**) on the surface of some immune cells, has shown encouraging results in patients with cervical cancer *(Hollebecque et al. 2017)*. **Pembrolizumab**, which is also a **PD-1** inhibitor, was recently approved for use as a treatment for cervical cancer in the US, based on the results of recent **clinical trials**. **Pembrolizumab** is approved in the US for use in patients with recurrent or metastatic cervical cancer that has progressed after **chemotherapy** treatment, and whose **tumours** have high levels of a protein called **programmed death-ligand 1** (**PD-L1**) *(Keytruda PI, 2018)*.

You have the right to accept or refuse participation in a **clinical trial** without any consequences for the quality of your treatment. If your doctor does not ask you about taking part in a **clinical trial** and you want to find out more about this option, you can ask your doctor if there is a trial for your type of cancer taking place nearby *(ClinicalTrials.gov 2017)*.

Supplementary interventions

Patients may find that supplementary care helps them to cope with their diagnosis, treatment and the long-term effects of cervical cancer

Over the course of disease, anti-cancer treatments should be supplemented with interventions aimed at preventing the complications of disease and treatment, and maximising your quality of life. These interventions may include supportive, palliative, survivorship and end-of-life care, which should all be coordinated by a multidisciplinary team (Jordan et al. 2018). Ask your doctor or nurse about which supplementary interventions are appropriate; you and your family may receive support from several sources, such as a dietician, social worker, physiotherapist, priest, occupational therapist or **lymphoedema** therapist.

Supportive care

Supportive care involves the management of cancer symptoms and the side effects of therapy.

Palliative care

Palliative care is a term used to describe care interventions in the setting of advanced disease, including the management of symptoms as well as support for coping with **prognosis**, making difficult decisions and preparation for end-of-life care. **Palliative care** in women with advanced cervical cancer often includes treatment for pain, vaginal discharge, **fistulae**, vaginal bleeding, diarrhoea, incontinence, nutritional problems, leg swelling and bedsores.

Survivorship care

Support for patients surviving cancer includes social support, education about the disease and rehabilitation. For example, psychological support can help you to cope with any worries or fears. Psychosocial problems impacting your quality of life may include mood and stress disorders, body image and fear of **recurrence** *(Pfaendler et al. 2015)*. Patients often find that social support is essential for coping with the cancer diagnosis, treatment and the emotional consequences. A survivor care plan can help you to recover wellbeing in your personal, professional and social life. For further information and advice on survivorship, see ESMO's patient guide on survivorship (ESMO 2017) (http://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship).

End-of-life care

End-of-life care for patients with incurable cancer primarily focusses on making the patient comfortable and providing adequate relief of physical and psychological symptoms, for example palliative sedation to induce unconsciousness can relieve intolerable pain, **dyspnoea**, delirium or convulsions *(Cherny 2014)*. Discussions about end-of-life care can be very distressing, but support should always be available to you and your family at this time.

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 about any potential side effects that are worrying you.

Doctors classify side effects from any cancer therapy by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, grade 1 side effects are considered to be mild, grade 2 moderate, grade 3 severe and grade 4 very severe. However, the precise criteria used to assign a grade to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your doctor as soon as possible.

It is important to talk to your doctor about any treatment-related 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 can provide you with strategies to limit the impact of **fatigue**, including getting enough sleep, eating healthily and staying active *(Cancer.Net 2016)*. Loss of appetite and weight loss can also arise due to the cancer itself or the treatments. Significant weight loss, involving loss of both fat and muscle tissue, can lead to weakness, reduced mobility and loss of independence, as well as anxiety and depression *(Escamilla and Jarrett 2016)*. Your doctor may refer you to a dietician, who can assess your nutritional needs and advise you on your diet and any supplements that you might need.

Surgery

Following surgery for cervical cancer, you may experience vaginal bleeding (similar to a light period), which can last for a few days to a few weeks. Some women also have irregular or painful periods after a **trachelectomy** – tell your doctor if your periods don't return to normal after the **trachelectomy**. Some women find they have problems emptying their bladder after having a radical **trachelectomy** or **hysterectomy** and have to use a **catheter** for a few weeks. It is important to rebuild your pelvic floor strength after surgery to prevent side effects such as loss of bladder control, decreased sexual satisfaction and poor abdominal strength. Your doctor or nurse will be able to advise you on pelvic floor exercises and how soon after surgery to start them.

continued overleaf

Lymphoedema can occur in the legs if **lymph nodes** have been removed. You can reduce your risk of **lymphoedema** in several ways:

- Maintain a healthy body weight to reduce the strain on your **lymphatic system**.
- Exercise regularly to encourage lymphatic drainage.
- Protect your skin to avoid infection.
  - Moisturise the skin in the area to prevent cracked skin.
  - Use sunscreen to prevent sunburn.
  - Apply insect repellent to prevent bites.

If you notice any signs of swelling or infection, tell your doctor as soon as possible.

Radiotherapy

The immediate side effects of external beam pelvic **radiotherapy** are usually due to the effects of radiation on the organs surrounding the **cervix** and **uterus**. Common side effects of **radiotherapy** include **fatigue**, skin irritation, bladder inflammation, vaginal bleeding, vaginal dryness and diarrhoea. **Radiotherapy** can also cause **lymphoedema** and permanent skin changes, including hardening of the skin and broken blood vessels. The main side effects associated with **brachytherapy** affect the **cervix** and wall of the **vagina**, most commonly irritation of the **vagina** and **vulva**, vaginal dryness and the feeling of a less flexible and/or shorter **vagina**.

It is important to look after your skin during **radiotherapy** treatment to prevent infection and reduce pain. Let your doctor or nurse know of any symptoms as he/she may be able to help. Rarely, tissue damaged during **radiotherapy** is unable to heal because the surrounding blood vessels are not able to supply enough oxygen to the damaged area. In these cases, **hyperbaric oxygen treatment** might be used to increase the amount of oxygen in your body, which increases the oxygen reaching the healing area. Vaginal lubricants and dilators can help to reduce vaginal dryness, shortening and stiffness *(Faithfull and White 2008)*. Ask your doctor or nurse about the products available and how to use them.

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. You may also experience some side effects that are not listed below. 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). Some patients find that their sense of taste is affected – changes in enzymes in your mouth can lead to a metallic taste and blisters. Reductions in your levels of **neutrophils** (a type of white blood cell) can lead to **neutropenia**, which can 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 will help you to manage them *(Macmillan 2016)*. The table below lists the most common side effects of **chemotherapy** drugs that may be used in the treatment of cervical cancer.

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Carboplatin (Macmillan 2015)	• **Anaemia** • Constipation • **Fatigue** • **Hepatic** (liver) toxicity • Increased risk of infection • Nausea • **Neutropenia** • **Renal** (kidney) toxicity • **Thrombocytopenia** • Vomiting	• 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 or nurse 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
Cisplatin (Macmillan 2016)	• **Anaemia** • **Anorexia** • Changes in kidney function • Decreased fertility • Diarrhoea • **Fatigue** • Increased risk of infection • Increased risk of **thrombosis** • Nausea/vomiting • **Neutropenia** • **Peripheral neuropathy** • Taste changes (metallic, salty or bitter tastes) • **Stomatitis** • **Thrombocytopenia** • **Tinnitus**/changes in hearing	• 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 • Effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea, taste changes) may result in loss of appetite (**anorexia**). Your doctor or nurse will be able to help you to prevent or manage these side effects • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor or nurse, who will help you to manage this side effect • You will have tests before and during treatment to check how well your kidneys are functioning. You will be asked to drink plenty of fluids to prevent your kidneys from becoming damaged • Tell your doctor or nurse if you notice any changes in your hearing or experience **tinnitus**. Changes in hearing are usually temporary but can occasionally be permanent • To prevent and treat **stomatitis**/**mucositis**, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (grade 2 and above) **stomatitis**, your doctor may suggest lowering the dose of treatment, or delaying therapy until the **stomatitis** resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Paclitaxel (Paclitaxel SPC, 2017)	• **Alopecia** • **Anaemia** • **Arthralgia** • Bleeding • Diarrhoea • Hypersensitivity reactions • Increased infections • **Leukopenia** • Low blood pressure • **Mucositis** • **Myalgia** • Nausea • **Neutropenia** • **Peripheral neuropathy** • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia**, **leukopenia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results and will advise you on how to prevent infections • Report any effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea) to your doctor or nurse as they may be able to help you to prevent or manage these side effects • Let your doctor or nurse 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 or nurse, who will help you to manage this side effect • To prevent and treat **stomatitis/mucositis**, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (grade 2 and above) **stomatitis**, your doctor may suggest lowering the dose of treatment, or delaying therapy until the **stomatitis** resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment • **Alopecia** can be upsetting for many patients; your doctor or nurse will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Topotecan (Hycamtin SPC, 2017)	• Abdominal pain • **Alopecia** • **Anaemia** • **Anorexia** • **Asthenia** • Constipation • Diarrhoea • **Fatigue** • Fever • Infection • **Leukopenia** • **Mucositis** • Nausea • **Neutropenia** • **Thrombocytopenia** • Vomiting	• 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 **granulocyte colony-stimulating factor** under the skin. It encourages the b**one marrow** (where blood cells are made) to make more white blood cells • To prevent and treat **stomatitis/mucositis**, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (grade 2 and above) **stomatitis**, your doctor may suggest lowering the dose of treatment, or delaying therapy until the **stomatitis** resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment • 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 • **Alopecia** can be upsetting for many patients; your doctor or nurse will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss

Important side effects associated with individual chemotherapy drugs used in the treatment of cervical cancer*. The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Targeted therapies

Many common side effects in patients treated with **bevacizumab** are similar to side effects from **chemotherapy** and include effects on the **gastrointestinal system** (e.g. diarrhoea, vomiting, nausea), **bone marrow** (e.g. **neutropenia**, **leukopenia**, **thrombocytopenia**) or more general effects like **fatigue**, but there can also be some more unusual side effects such as skin reactions and **hypertension** (high blood pressure). Many of the side effects from **bevacizumab** can be prevented or managed effectively. Always tell your doctor as soon as possible if you notice any side effects from taking **bevacizumab**. The table below lists the most common side effects of **bevacizumab**.

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Bevacizumab (Avastin SPC, 2017)	• **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	• 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 • Let your doctor or nurse know if you experience a persistent cough. Troublesome **dyspnoea** can be treated with drugs called opioids or benzodiazepines, and in some cases steroids are used *(Kloke and Cherny 2015)* • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor or nurse, 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 or nurse will be able to help you to prevent or manage these side effects • To prevent and treat **stomatitis/mucositis**, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (grade 2 and above) **stomatitis**, your doctor may suggest lowering the dose of treatment, or delaying therapy until the **stomatitis** resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment • Let your doctor or nurse 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, **dysarthria** (difficulty with speech), **arthralgia** (painful joints) or headache to your doctor or nurse, who will help you to manage these side effects

Important side effects associated with targeted therapies in the treatment of cervical 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, including an examination of the pelvic and rectal area. Some patients might also have a **CT** or **PET/CT scan** – your doctor will discuss this with you. Your doctor will let you know how often you need to return for further follow-up appointments, but a typical follow-up schedule would involve check-ups every 3–6 months in the first 2 years after treatment, every 6–12 months after 3 years and annually after 5 years *(Marth et al. 2017)*.

What if I need more treatment?

Despite the best possible treatment at diagnosis, there is still a possibility that your cancer may return. 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 in the pelvis following primary surgery, you may be offered **radiotherapy** or **pelvic exenteration** (removal of the bladder, part of the bowel, **ovaries**, **uterus**, **cervix** and **vagina**). Recurrent **tumours** in distant organs are regarded as metastatic cancers and you may be offered **chemotherapy** and **targeted therapy** (see section 'What are the treatment options for metastatic cervical cancer?' for more information).

Looking after your health

After you have had treatment for cervical cancer, you may feel very tired and emotional. Give your body time to recover and make sure you get enough rest, but there is no reason to limit activities if you are feeling well. 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. 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.

The following eight recommendations form a good foundation for a healthy lifestyle after cancer *(Wolin et al. 2013)*:

- Don't smoke
- Avoid second-hand smoke
- Exercise regularly
- Avoid weight gain
- Eat a healthy diet
- Drink alcohol in moderation (if at all)
- Stay connected with friends, family and other cancer survivors
- Attend regular check-ups and screening tests

A healthy, active lifestyle will help you to recover physically and mentally

Regular exercise is an important part of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. In cancer survivors, exercising regularly (e.g. 30 minutes five times a week) can improve physical function, fitness, strength, cancer-related **fatigue**, depression and quality of life *(Lin et al. 2016)*. It is estimated that only a third of cervical cancer survivors are getting enough exercise *(Pennington and McTiernan 2018)*, so it is very important that you listen carefully to the recommendations of your doctor or nurse, and talk to them about any difficulties you have with exercise.

Long-term effects

After completing treatment for cervical cancer, you may experience some long-term side effects, depending on the treatment you have received.

Pelvic **radiotherapy** can cause scarring in the lining of the large bowel and weakening of rectal muscles, resulting in long-term bowel symptoms such as diarrhoea, constipation, incontinence or bleeding from the rectum. **Radiotherapy** can also cause long-term effects on the **urinary tract** *(Liberman et al. 2014)*, as well as **lymphoedema** up to 1–2 years after treatment, and body image and sexual problems as long as 5 years after treatment *(Dieperink et al. 2018)*. Permanent skin changes, difficulty with bowel and bladder control, chronic pain and hot flushes are all common long-term effects of **radiotherapy**, which can also result in women feeling less feminine and dissatisfied with their bodies. Permanent tattoos in the vulval area, which are drawn onto the skin to ensure the **radiotherapy** is directed to the correct area, may also affect body image. Tightening and shortening of the **vagina** due to scarring from **radiotherapy**, combined with vaginal dryness, pain and bleeding during or after sex, may also lead to a lack of sexual desire long after **radiotherapy** treatment is complete *(Khalil et al. 2015)*.

Radical surgery to remove the **tumour** may mean that the bowel and/or bladder are damaged, and a permanent **stoma** (a small opening on the surface of the abdomen to direct faeces and/or urine into an external **stoma** bag) may be necessary *(Hsu et al. 2012)*. Having a **hysterectomy** can increase the risk of **urinary incontinence** and **vaginal prolapse** years after surgery due to damage to the supporting pelvic floor muscles. If the **ovaries** are removed, menopause will be triggered in women who have not already experienced it.

As well as physical effects, psychosocial problems such as mood and stress disorders, body image anxiety and fear of **recurrence** may affect you long after your treatment has ended *(Pfaendler et al. 2015)*. You may be unsure if you are able to endure the stress of returning to work, but this can provide an opportunity to reconnect with colleagues and is a source of self-worth and purpose for many people. You may also be concerned about loss of fertility or your ability to maintain a pregnancy; however, there may be alternative options if you are no longer able to conceive naturally, including assisted reproduction techniques.

The long-term effects of cervical cancer and its treatment can be managed so it is important that you tell your doctor or nurse about any persistent or new symptoms. Your doctor or nurse will also work with you to develop a personalised survivorship care plan.

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 patient advocacy groups, which help patients and their families to navigate the cervical 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 cervical cancer.

For further information about ENGAGE, and to find details of patient advocacy groups in your area, visit: https://engage.esgo.org/

References

Cancer.Net. 2016. Fatigue. Available from: http://www.cancer.net/navigating-cancer-care/side-effects/fatigue. Accessed 12th October 2017.

Cherny NI. ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation. Ann Oncol 2014;25(suppl 3):iii143-52.

ClinicalTrials.gov. 2017. Learn about clinical studies. Available from: https://clinicaltrials.gov/ct2/about-studies/learn. Accessed 30th November 2017.

Cordeiro CN and Gemignani ML. Gynecologic malignancies in pregnancy: Balancing fetal risks with oncologic safety. Obstet Gynecol Surv 2017;72(3):184-193.

Dieperink KB, Sigaard L, Larsen HM, Mikkelsen TB. Rehabilitation targeted late adverse effects after radiotherapy for cervical cancer: different gains in different settings. Clin Nurs Studies 2018;6:9-16.

Escamilla, DM and P Jarrett. The impact of weight loss on patients with cancer. Nurs Times 2016;112:20-22.

Faithfull S, White I. Delivering sensitive health care information: challenging the taboo of women's sexual health after pelvic radiotherapy. Patient Educ Couns 2008;71(2):228-33.

Ferlay J, Soerjomataram I, Ervik M, et al. et al. 2013. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from: http://globocan.iarc.fr. Accessed 10th October 2017.

Halaska M, Robova H, Pluta M, Rob L. The role of trachelectomy in cervical cancer. Ecancermedicalscience 2015;9:506.

Hollebecque A, Meyer T, Moore KN, et al. An open-label, multicohort, phase I/II study of nivolumab in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in recurrent or metastatic (R/M) cervical, vaginal, and vulvar cancers. J Clin Oncol 2017;15(suppl):5504-5505.

Hsu TC, Huang TM, Yang YC. A surgeon's help with the management of bowel problems related to gynecology is truly needed - comparison of two periods spanning 24 years. Taiwan J Obstet Gynecol 2012;51:612-615.

Jordan K, Aapro M, Kaasa S, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. Ann Oncol 2018;29:36-43.

Khalil J, Bellefqih S, Sahli N, et al. Impact of cervical cancer on quality of life: beyond the short term (Results from a single institution): Quality of life in long-term cervical cancer survivors: results from a single institution. Gynecol Oncol Res Pract 2015;2:7.

Kloke M and Cherny N. Treatment of dyspnoea in advanced cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol 2015;26(Suppl 5):v169-v173.

Liberman D, Mehus B, Elliott SP. Urinary adverse effects of pelvic radiotherapy. Transl Androl Urol 2014;3(2):186-195.

Lin KY, Frawley HC, Denehy L, et al. Exercise interventions for patients with gynaecological cancer: a systematic review and meta-analysis. Physiotherapy 2016;102(4):309-319.

Macmillan. 2015. Carboplatin. Available from: https://www.macmillan.org.uk/cancerinformation/cancertreatment/treatmenttypes/chemotherapy/individualdrugs/carboplatin.aspx. Accesssed 12th October 2017.

Macmillan. 2016. Cisplatin. Available from: https://www.macmillan.org.uk/information-and-support/treating/chemotherapy/drugs-and-combination-regimens/individual-drugs/cisplatin.html#320670. Accessed 24th April 2018.

Macmillan. 2016. Possible side effects of chemotherapy. Available from: http://www.macmillan.org.uk/information-and-support/lung-cancer/non-small-cell-lung-cancer/treating/chemotherapy/side-effects-of-chemotherapy/possible-side-effects.html. Accessed 12th October 2017.

Marth C, Landoni F, Mahner S, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28(Suppl 4):iv72-iv83.

Pennington KP, McTiernan A. The role of physical activity in breast and gynecologic cancer survivorship. Gynecol Oncol 2018;149(1):198-204.

Pfaendler KS, Wenzel L, Mechanic MB, Penner KR. Cervical cancer survivorship: long-term quality of life and social support. Clin Ther 2015;37(1):39-48.

Wolin KY, Dar H, Colditz GA. Eight ways to stay healthy after cancer: an evidence-based message. Cancer Causes Control 2013;24:827-837.

GLOSSARY

ADENOCARCINOMA
Cancer that begins in glandular (secretory) cells

ADJUVANT (TREATMENT)
Additional treatment given after the primary treatment to reduce the chance of the cancer coming back; usually refers to **radiotherapy** and/or **chemotherapy** after surgery

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
Joint pain

ASTHENIA
Abnormal feeling of weakness or lack of energy

BEVACIZUMAB
A type of **targeted therapy** used to treat some cancers, including advanced cervical 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

BIOPSY
A medical procedure in which a small sample of cells or tissue is taken for examination under a microscope

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

BRACHYTHERAPY
A type of **radiotherapy** in which the radioactive source is placed directly into or near a **tumour**

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

CATHETER
A flexible tube used to empty the bladder and collect urine in a drainage bag

CERVICAL INTRA-EPITHELIAL NEOPLASIA (CIN)
Abnormal cells on the surface of the **cervix**. CIN is not cancer, but may develop into cancer

CERVIX
The low, narrow end of the **uterus** that forms a canal between the **uterus** and **vagina**

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

CHEMORADIOTHERAPY
Chemotherapy and **radiotherapy** given together

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

CLINICAL TRIAL
A study that compares the effects of one treatment with another

COLD CAP
A cap that cools the scalp before, during and after treatment to reduce the effects of the treatment on **hair follicles**

COLPOSCOPY
A procedure in which a lighted, magnifying instrument called a colposcope is used to examine the **cervix**, **vagina** and **vulva**

COMPUTED TOMOGRAPHY (CT) SCAN
A scan using **x-rays** and a computer to create detailed images of the inside of your body

CONISATION
A procedure in which a cone-shaped piece of abnormal tissue is removed from the **cervix**

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

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

DYSGEUSIA
A change in the sense of taste

DYSPNOEA
Shortness of breath

GLOSSARY

ENDOCERVICAL CHANNEL
The inner part of the **cervix** that forms a canal that connects the **vagina** to the **uterus**

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

FATIGUE
Overwhelming tiredness

FERTILITY-SPARING (SURGERY)
A procedure used to help preserve a woman's ability to have children

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

FISTULAE
Abnormal openings or passages between two organs; in cervical cancer, **fistulae** can develop between the bladder and the **vagina**, leading to a persistent discharge of fluid from the **vagina**

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

GRANULOCYTE COLONY-STIMULATING FACTOR
A drug used to treat **neutropenia**

GENERAL ANAESTHETIC
A medication that causes a reversible loss of consciousness

HAIR FOLLICLE
A small sac in the skin from which hair grows

HEPATIC
Relating to the liver

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

HUMAN PAPILLOMAVIRUS (HPV)
A type of virus that can cause abnormal tissue growth and other changes to cells. Infection for a long time with certain types of **HPV** can cause cervical cancer

HYDRONEPHROSIS
Abnormal enlargement of a kidney

HYPERBARIC OXYGEN TREATMENT
Treatment involving breathing pure (100%) oxygen under increased pressure. This allows extra oxygen to be taken up by the bloodstream and dissolved quickly. The extra oxygen can help where healing is slowed down by infection or where blood supply is limited by damage to the tissues

HYPERTENSION
Abnormally high blood pressure

HYSTERECTOMY
Surgery to remove the **uterus** and **cervix**

IONISING RADIATION
Any type of particle or electromagnetic wave that carries enough energy to ionise or remove electrons from an atom (e.g. **x-rays**)

IMMUNOTHERAPY
A type of cancer treatment that stimulates the body's immune system to fight the cancer

INTRAVENOUS
Administered into a vein

INTRAVENOUS PYELOGRAM
X-ray examination that uses a special dye to view the **urinary tract** in detail

LAPAROSCOPY
A procedure that involved the insertion of a thin, tube-like instrument with a light and a lens for viewing (laparoscope) through the abdominal wall to examine the inside of the abdomen and/or remove tissue

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

LOOP ELECTROSURGICAL EXCISION
A technique that uses electric current passed through a thin wire loop to remove abnormal tissue

LYMPHATIC SYSTEM
A network of tissues and organs that help rid the body of toxins, waste and other unwanted materials. The primary function of the **lymphatic system** is to transport lymph, a fluid containing infection-fighting white blood cells, throughout the body

GLOSSARY

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

LYMPHOEDEMA
Swelling caused by a build-up of lymph fluid in the tissues of the body. This may result from damage to the **lymphatic system** because of surgery or **radiotherapy** to the **lymph nodes** in the pelvis

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

LYMPHOVASCULAR INVASION
Spread of a cancer to the blood vessels and/or **lymphatic system**

MARGIN
The edge or border of the tissue removed in cancer surgery. The **margin** is described as negative or clean when no cancer cells are found at the edge of the tissue, suggesting that all of the cancer has been removed. The **margin** is described as positive or involved when cancer cells are found at the edge of the tissue, suggesting that all of the cancer has not been removed

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

MAGNETIC RESONANCE IMAGING (MRI) SCAN
A type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body

MUCOSA
The moist, inner lining of some organs and body cavities

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

MYALGIA
Muscular pain

NEOADJUVANT (TREATMENT)
Treatment given as a first step to shrink a **tumour** before the main treatment (usually surgery) is given

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

NIVOLUMAB
A type of **immunotherapy** that blocks a protein called **PD-1** on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

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

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

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

PALLIATIVE (CARE)
The care of patients with advanced, progressive illness. It focuses on providing relief from pain, symptoms and physical and emotional stress, without dealing with the cause of the condition

PAPANICOLAOU (PAP) TEST
A procedure in which a small brush or spatula is used to gently remove cells from the **cervix** so they can be checked under a microscope for cervical cancer or cell changes that may lead to cervical cancer

PARAMETRIAL
Referring to the fat and connective tissue surrounding the **uterus**

PELVIC EXENTERATION
An operation to remove the bladder, part of the bowel, **ovaries**, **uterus**, **cervix** and **vagina**

PEMBROLIZUMAB
A type of **immunotherapy** that blocks a protein called **PD-1** on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It 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

GLOSSARY

POSITRON EMISSION TOMOGRAPHY (PET)
An imaging test that uses a dye with radioactive tracers, which is injected into a vein in your arm

PLATINUM-BASED
A class of **chemotherapy** that includes **cisplatin** and **carboplatin**

PROGNOSIS
The likely outcome of a medical condition

PROGRAMMED CELL DEATH PROTEIN 1 (PD-1)
A cellular protein thought to be involved in helping the **tumour** to evade detection by the body's immune system

PROGRAMMED DEATH-LIGAND 1 (PD-L1)
A cellular protein thought to be involved in helping the **tumour** to evade detection by the body's immune system

RADIOTHERAPY
Treatment involving the use of high-energy radiation, which is commonly used to treat cancer

RECURRENCE
Return of a cancer

RENAL
Relating to the kidneys

RHINITIS
Inflammation of the lining inside the nose

SENTINEL LYMPH NODE DISSECTION (SLND)
Removal and examination of the sentinel node(s) – the first **lymph node(s)** to which cancer cells are likely to spread from a primary **tumour**

SQUAMOUS (CELLS)
Thin, flat cells that are found in the tissue that forms the surface of the skin, the lining of hollow organs of the body, and the lining of the respiratory and digestive tracts

STOMA
A surgically-created opening from an area inside the body to the outside

STOMATITIS
Inflammation of the inside of the mouth

STROMAL INVASION
The spread of cancer into underlying muscle and connective tissues

SYSTEMIC (THERAPY)
Drugs that spread throughout the body to treat cancer cells wherever they may be. They include **chemotherapy**, **targeted therapy** and **immunotherapy**

TARGETED THERAPY
A newer type of drug that works by blocking the signals that tell cancer cells to grow or by interfering with their ability to obtain nutrients for growth

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

THROMBOSIS
The formation of a blood clot inside a blood vessel, obstructing the flow of blood through the blood system

TINNITUS
The hearing of a sound (such as ringing, whining or buzzing) when no external sound is present

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

TRACHELECTOMY
Surgery to remove the **cervix**. The upper part of the **vagina** and some pelvic **lymph nodes** may also be removed

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

URINARY INCONTINENCE
Inability to control the flow of urine from the bladder

URINARY TRACT
The organs of the body that produce and discharge urine, including the kidneys, ureters, bladder and urethra

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

VAGINAL PROLAPSE
A condition in which one or more of the organs in the pelvis (**uterus**, bowel, bladder or top of the **vagina**) slip down from their normal position and bulge into the **vagina**

GLOSSARY

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)
A protein produced by cells that stimulates the growth of new blood vessels

VULVA
The external female genital organs

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 cervical cancer and the treatments that are available. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of cervical 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 cervical cancer.

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

European Society for Medical Oncology (ESMO)
Via Ginevra 4
6900 Lugano
Switzerland

Tel: +41 (0)91 973 19 99
Fax: +41 (0)91 973 19 02
E-mail: clinicalguidelines@esmo.org

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

We can help you understand cervical 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**