



➔ ENDOMETRIAL CANCER FACTSHEET

What is endometrial cancer?



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Introduction

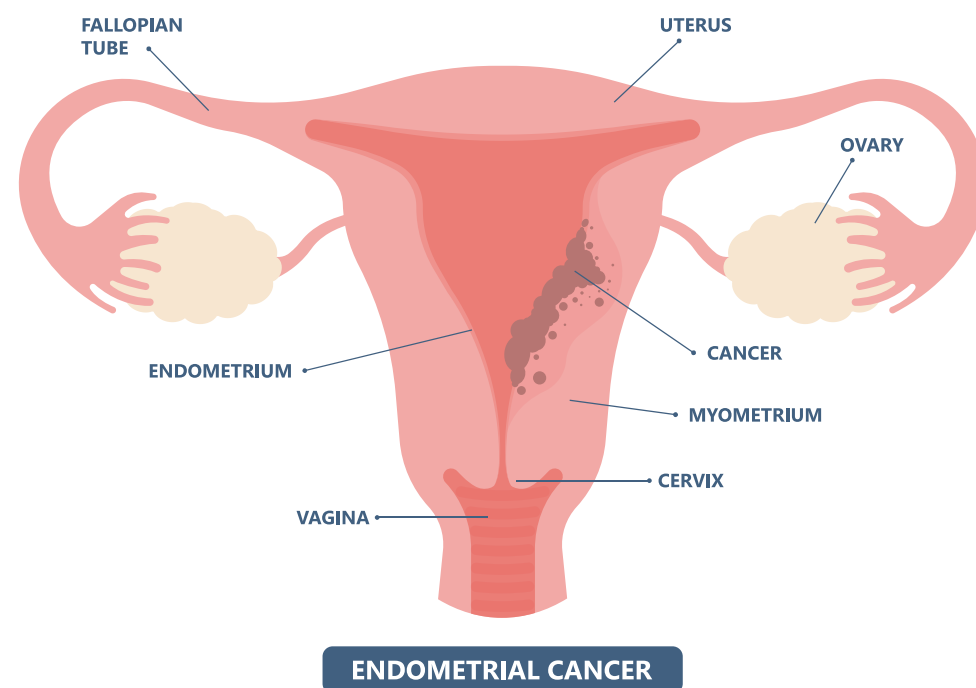
ENGAGe is proud to present the very first European brochure for women with endometrial cancer based on the newest insights of the research and best clinical practices.

For many years, women with endometrial cancer were not the focus in clinical and scientific praxis. Based on the newest insights of the tumour biology of endometrial cancer and the positive results of international clinical trials, there are new and better treatment options available for women with endometrial cancer.

This brochure aims to support you in the dialogue with your physicians and to motivate you to ask open questions because information and knowledge is the backbone for the very best management of cancer.

What is endometrial cancer?

Endometrial cancer has become the most common gynaecological cancer in Europe. It affects women with an average age of diagnosis of 69 but can also occur earlier. This type of cancer arises from the inner layer of the uterus, the “endometrium”. The terms “uterine cancer” and “endometrial cancer” are often used synonymously. Functionally, the endometrium consists of two layers, a basal and a functional layer. The latter thickens and is then shed during the menstruation. This happens under the influence of several hormones like oestrogen and progesterone. The uterus, also called womb, is an inverted pear-shaped muscular organ of the female reproductive system, located between the bladder and the rectum.



The incidence of endometrial cancer rose significantly in the last decade. The calculated number of new cases in Europe in 2020 was 130,051.⁽¹⁾ Overall, this type of cancer has a good prognosis due to its predominantly early diagnosis.

In contrast to cervical cancer, there is no established screening method for endometrial cancer. The PAP smear test for detection pathologies of the cervix is not able to detect endometrial cancer. However, it might show signs of abnormal endometrium in certain cases.⁽²⁾

What are the different types of endometrial cancer?

Previously, this type of cancer was divided only into “type 1” and “type 2” cancers.

Type 1 cancer is found in the majority (80%) and is related to an excess of oestrogen in the body, whereas **Type 2 cancer** is more aggressive, faster growing, and not oestrogen-related.

However, recent research findings improved the classification significantly and helped to better identify patients with higher risk for recurrence or higher need of chemotherapy or no chemotherapy. The classification is based on immunohistochemical or molecular markers, which means that the tissue is tested for specific markers or undergoes extensive testing for anomalies. Based on the European Guidelines for the Management of Patients with Endometrial Carcinoma⁽²⁾, this classification should be the basis for every treatment recommendation.

New FIGO 2023 classification for endometrial cancer

The so-called FIGO (International Federation of Gynaecology and Obstetrics) is an organization that covers many fields in women’s health including staging systems for cancer patients. According to pathological findings, every gynecological cancer can be categorized into a “stage” which usually has a direct impact on the treatment. Due to recent new findings in the immunohistochemical classification of endometrial cancer, it was necessary to update this classification. The updated FIGO classification was published in 2023. It ensures a tailored treatment for patients with endometrial cancer and has a direct influence on the cancer prognosis, too. Furthermore, with the integration of tumor grade and biomolecular classification data, the treatment approach aligns more closely with the choice of adjuvant therapy e.g. after surgery. The newly integrated immunohistological findings should already be present within the first diagnosis e.g. after hysteroscopy and/or sampling with curettage.

We would recommend directly asking your physician to explain to you in detail what this could mean for your treatment or to directly contact an ESGO-certified Center of Excellence.

How is endometrial cancer diagnosed?

» SYMPTOMS

The most common symptom is postmenopausal vaginal bleeding, which is vaginal bleeding of any intensity that occurs a year or more after the last menstrual period. However, especially in younger women, abnormal bleeding (e.g., bleeding between periods without any other cause) and pelvic pain can be warning symptoms.

Warning symptoms

- Postmenopausal bleeding
- Pelvic and abdominal pain
- Abdominal tension
- Diarrhoea or severe constipation
- Vaginal discharge
- Premenopause abnormal bleeding between periods or a very long and heavy period (not related to non-malignant uterine diseases or hormonal disorders)

» EXAMINATIONS

Expert Advice

*A biopsy is required for the diagnosis of endometrial cancer.
An adequate evaluation is also relevant for planning the best surgical approach.*

If one of the above-mentioned symptoms occurs regularly, consult your gynaecologist without delay.

The following examinations should be done:

1/ General examination (e.g., lymph nodes, abdomen, extremities)

- **Vaginal examination**, biannually including inspection of the cervix
- **Transvaginal ultrasound** to examine endometrial thickness, the cavity, the size and form of the uterus, the ovaries and the rectouterine cul-du-sac
- **Transabdominal ultrasound of the kidneys, liver, spleen** (and check for free fluid)

2/ If cancer or pathological findings are suspected, further tests are necessary:

- **Hysteroscopy**: The doctor examines the womb with a camera. This procedure can be done without anaesthesia as an "Office Hysteroscopy" or under sedation / light sleep
- **Biopsy**: It is necessary to take a probe of the endometrial layer by removing tissue with a curettage; this can also be done with new small instruments (e.g., pipelle curettage or office hysteroscopy)
- **In some cases, further imaging is indicated**, including computer tomography, or magnetic resonance imaging as well cystography and/or rectoscopy.

In the case of invasive diagnostics, the probe will be seen by a pathologist under a microscope.

Risk factors and genetic risk

Uterine cancer is very often associated with several risk factors. Nevertheless, endometrial cancer can also occur without these risk factors.

Some of them include individual parameters, others are related to medication; for example, the use of hormonal medication. It is important to know that patient-related risk factors can be modified and improved which may help to treat the patient in the most optimal way and might therefore be associated with better prognosis.

The following risk factors are well known:

- **Age**
- **Obesity** (fatty tissue can produce oestrogen), **Type II Diabetes mellitus**
- **Use of tamoxifen**, a drug mainly used in the treatment of breast cancer
- **Genetics**: people in families with Lynch syndrome have a significantly higher risk

What is Lynch syndrome?

Lynch syndrome used to be called HNPCC = hereditary nonpolyposis colorectal cancer (HNPCC).

Families with Lynch syndrome have risks for several malignancies, including colon cancer, endometrial cancer, and ovarian cancer, but also other cancers, such as gastric cancer ⁽³⁾, small bowel, pancreatic, prostate, urinary tract, kidney, bile duct and brain cancers.

Generally, patients with Lynch syndrome suffer from cancer diagnosis at an earlier age than other patients.

Family history is crucial; therefore, the dialogue with your doctors is essential.

Most guidelines recommend a systematic evaluation of the presence of Lynch syndrome, using a checklist to identify patients with a special risk, and offering genetic counselling as routine.

The modern treatment of endometrial cancer

Based on the results of international trials, there are various treatment modalities for women with endometrial cancer available. They include surgery, radiation, chemotherapy, antihormonal therapy, and immunotherapy.

The backbone for every treatment recommendation should be the newest guidelines and should be discussed in an interdisciplinary tumour board meeting to define the best, individualised treatment plan.

There are several factors that influence the treatment decision-making process, such as pathological findings, including molecular pathology, tumour stage, tumour margins, lymph node involvement, tumour pattern, previous therapy, symptoms, and co-morbidities.

Every medical intervention can cause side effects, in most cases these are well tolerated, and supportive therapies are available to prevent and treat side effects adequately.

The most common side effects include:

- intestinal complaints
- urinary complaints
- fatigue
- lymphoedema
- aches and pain in the abdomen due to scar tissue
- early menopause in younger women
- impact on sexual life
- psychological complaints

Expert Advice

Please describe to your medical staff every symptom and complaint, whether or not you believe this can be associated with the cancer or a specific therapy.

Participation in a clinical trial is regarded as an additional quality indicator.

Expert Advice

Please always ask your doctor about the possibility of participation in a clinical trial.

Many cases of endometrial cancer are diagnosed at an early stage. Therefore, the most common treatment is surgery. Depending on the final pathological evaluation, chemotherapy or radiation afterwards may be necessary.

Surgery

Surgery generally includes the removal of the uterus with both ovaries. This is mostly done via minimally invasive surgery such as laparoscopy or robotic surgery. In some cases, for example in advanced stage disease, the procedure is also done via an abdominal incision. Advanced surgery can also mean the removal of other organs like parts of the large bowel and should only be done in specialised centres.

The **lymph nodes** play a major role in treatment and are very important for the prognosis. The most important lymph nodes are those which are close to the large abdominal and pelvic vessels. If indicated, the lymph nodes along those vessels should be removed. However, newer techniques allow only the removal of “sentinel lymph nodes”, which represent the first node affected. The decision about the removal depends on tumour stage and tumour biology. Surgery is in general the cornerstone of the management of all types of endometrial cancer. In some cases, for patients who wish to become pregnant and are at an early cancer stage, an **antihormonal medication** can be applied as a fertility-sparing measure.

The discussion should be done in a certified gynaecological centre based on an adequate clinical and pathological evaluation and an accurate diagnosis.



Radiation

Radiation can be an option if surgery is not possible, for example, because of a less fit patient, if the tumour is locally advanced, or in cases of a large concentration of connective tissues. It is also possible in specific stages after surgery, in advanced stages, or in combination with chemotherapy. There are two approaches to irradiation, the **percutaneous** (from outside) and the **vaginal** (brachytherapy). Sometimes they are applied combined or sometimes only one approach is indicated based on special risk factors and the specific tumour pattern.

Chemotherapy and immunotherapy

➤➤ **Chemotherapy** is mainly platinum-based and is given in high-risk and advanced stage cancer and in recurrent disease. As previously mentioned, the new classification of endometrial cancer can help to better match patients to the types of systematic therapy.

➤➤ **Immunotherapy** basically means that the body's own immune system is used to attack cancer.

In this therapy, a type of new agent blocks specific proteins, so-called checkpoints that are made by some types of immune system cells (such as T cells), and some cancer cells. These checkpoints are used by the cancer cells to avoid detection by the immune system cells.

Several international trials have shown the efficacy of these non-chemotherapeutical approaches or in combination with chemotherapy in women with relapsed endometrial cancer. There are ongoing trials to investigate the benefit of these therapies in the primary diagnosis setting.

Expert Advice

Ask your gynaecologist or oncologist directly about innovative treatments and, together, find the optimal course of treatment for your specific medical situation and personal needs.

Antihormonal therapy

In some cases of relapsed endometrial cancer and the presence of hormonal receptors (oestrogen, progesterone) an anti-hormonal therapy (e.g., aromatase inhibitor) can be indicated.

ADC Therapy

The treatment of cancer has undergone tremendous progress over the past decades. In addition to traditional chemotherapy, so-called targeted therapies are gaining increasing importance, offering more gentle yet potentially more effective treatment options. One of the newest and most promising methods in this field is ADC therapy, or Antibody-Drug Conjugate treatment. This is essentially a form of targeted chemotherapy.

This therapy works like a “smart missile” within the body. It uses an antibody that can recognize specific proteins found on the surface of cancer cells. Once the antibody finds its target cell, it enters the cell and releases a powerful anticancer agent (the chemotherapy drug). This way, the treatment directly destroys the cancer cell while ideally sparing healthy tissues.

This approach is particularly promising for certain gynecologic cancers, such as ovarian cancer, cervical cancer, or some types of endometrial cancer, where tumor-specific targets (e.g., Trop-2, FR , or other specific proteins) can be identified. Some of them are now considered as validated options in selected indications of recurrent or resistant diseases. Many trials are now ongoing testing the interest of ADCs in adjuvant setting. ADCs are designed to be effective even in cases where other treatments—like chemotherapy—have failed or cause too many side effects.

Advantages of ADC Therapy

- **Highly targeted:** ADCs recognize only the target molecules on the surface of cancer cells, which may minimize damage to healthy cells.
- **Delivers powerful drugs exactly where they are most needed**, while sparing the rest of the body as much as possible.
- **May provide a new option for patients** for whom conventional treatments have not been effective.

Side Effects:

It is important to note that while ADC therapy is targeted, it is not entirely free of side effects. Small amounts of the drug may still reach healthy cells, and depending on individual sensitivity, unpleasant symptoms may occur. The type of side effects depends on the specific ADC used, but the most common may include:

- Fatigue and weakness
- Nausea and vomiting
- Diarrhea or constipation
- Changes in blood counts (e.g., decreased white blood cells)
- Skin rashes, hair loss
- In some types, neurological side effects or corneal problems may also occur

Cancer surveillance

Every woman with endometrial cancer should be offered a cancer surveillance program including close follow-up after the completion of treatment for endometrial cancer. This usually includes a detailed history and physical and gynaecological examination every three months within the first three years after the diagnosis and then every six months until the fifth year and then at least once in a year.

Cancer surveillance should also address social, and psychological aspects, optimal management of comorbidities (e.g., hypertonia, diabetes), possible late consequences of (cancer) treatment as well life-style aspects, such as nutrition and physical activity. Please consult other ENGAGe brochures that deal with all the above-mentioned topics at <https://engage.esgo.org/brochures/>

Expert Advice

Please ask your doctor about your personal cancer surveillance programme.

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ENGAGe would like to thank the authors, the contributors and ENGAGe Executive Group members for their constant availability and work on updating this factsheet.

ENGAGe wishes to express sincere gratitude to the authors Dr. Robert Armbrust (Germany) and Prof. Dr. Jalid Sehouli (Germany), as well as to external reviewer Dr. Zoia Razumova (Sweden) and to Marisska Jansen (Belgium) and Jolanda Wellen (Netherlands) for offering patient perspectives.

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ENGAGe recommends contacting your local patient association!

