

# Esophageal Cancer

What is  
esophageal  
cancer?

Let us explain  
it to you.

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# ESOPHAGEAL CANCER: A GUIDE FOR PATIENTS

## PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the nature of oesophageal cancer and appreciate the best treatment choices available according to the subtype of esophageal cancer. We recommend patients to ask their doctors what tests or types of treatments are needed for their type and stage of disease. 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 oesophageal cancer. This guide for patients has been produced in collaboration with ESMO and is disseminated with the permission of ESMO. It has been written by a medical doctor and reviewed by two oncologists from ESMO including the lead author of the clinical practice guidelines for professionals. It has also been reviewed by patients' representatives from ESMO's Cancer Patient Working Group.

More information about the Anticancer Fund: [www.anticancerfund.org](http://www.anticancerfund.org)

More information about the European Society for Medical Oncology: [www.esmo.org](http://www.esmo.org)

*For words marked with an asterisk, a definition is provided at the end of the document.*

## Table of content

Definition of esophageal cancer.....	3
Is esophageal cancer frequent? .....	4
What causes Esophageal cancer? .....	5
How is esophageal cancer diagnosed?.....	7
What is it important to know to get the optimal treatment? .....	9
What are the treatment options? .....	12
What are the possible side effects of the treatment? .....	19
What happens after treatment? .....	21
Definitions of difficult words.....	23

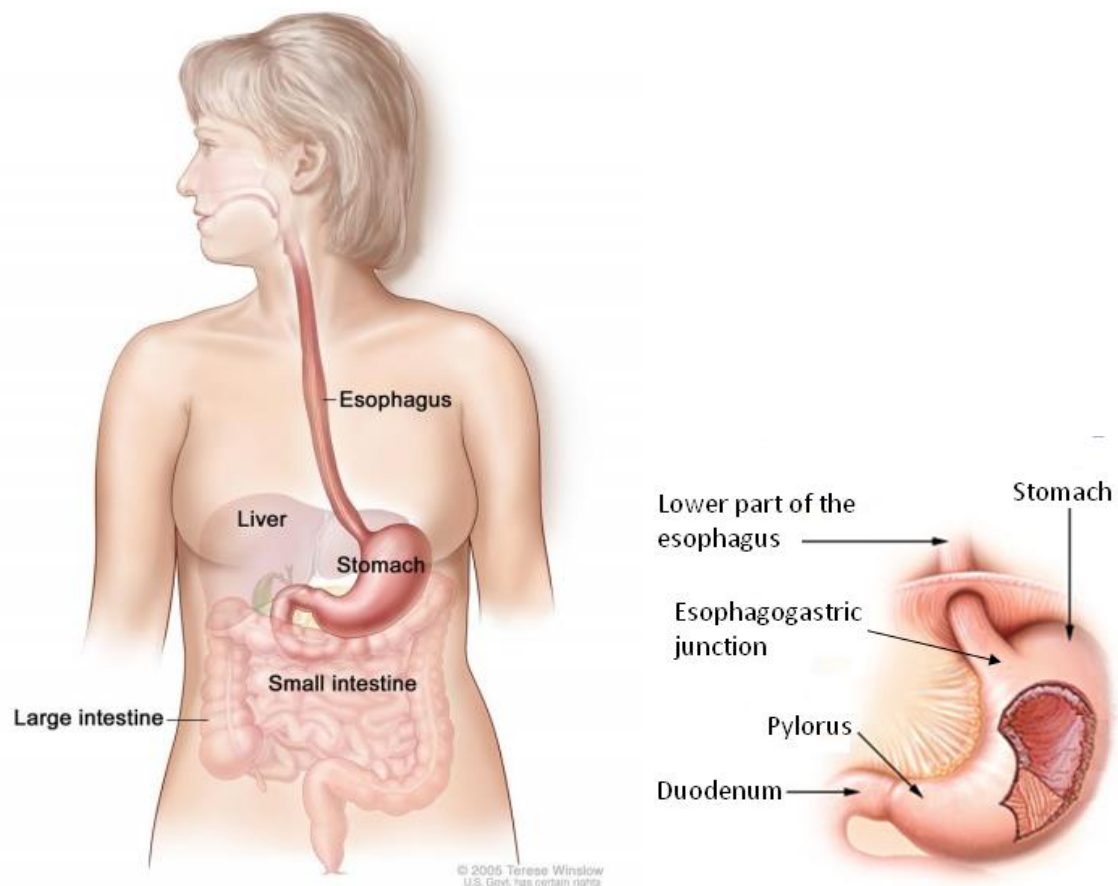
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## DEFINITION OF ESOPHAGEAL CANCER

*This definition is adapted from and is used with the permission of the National Cancer Institute (NCI) of the United States of America.*

Esophageal cancer is a tumor that forms in tissue lining the esophagus. The esophagus or gullet is the muscular tube through which food passes from the throat to the stomach.

The two main types of esophageal cancer are squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma is cancer that begins in flat cells lining the esophagus. Adenocarcinoma is cancer that begins in cells that produce and release mucus\* and other fluids. Both types occur at about the same frequency.



Anatomy of the digestive system (left) and anatomy of the lower esophagus, esophagogastric junction and stomach (right)

### Important note regarding another type of esophageal cancer

Small cell carcinomas are a very rare type of esophageal cancer. The information provided in this Guide for Patients does not apply to small cell carcinomas.

## IS ESOPHAGEAL CANCER FREQUENT?

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In Europe, about 5 to 10 in every 1,000 men and about 1 in every 1,000 women will develop esophageal cancer at some point in their life.

In 2008, about 35,000 men and about 10,000 women developed cancer of the esophagus in Europe. There are considerable differences between European countries. Esophageal cancer is more frequent in France and the UK and less frequent in Greece.

Squamous cell carcinomas are most prevalent in Asia, whereas adenocarcinomas are more prevalent and increasing rapidly in Western countries. Most esophageal cancers occur in people older than 65.

The discrepancies in the geographical distribution of the 2 main types, squamous cell carcinomas and adenocarcinomas, are due to the differences in the factors involved in their development. Squamous cell carcinomas are mainly associated with alcohol intake and smoking whereas adenocarcinomas are mainly associated with gastroesophageal reflux\* which is more related to obesity. This also explains the rapid increase of adenocarcinomas in western countries.

## WHAT CAUSES ESOPHAGEAL CANCER?

To this day, it is not clear why esophageal cancer occurs. However, some risk factors\* have been identified. A risk factor increases the risk of cancer occurring, but is neither necessary nor sufficient to cause cancer. A risk factor is not a cause in itself.

**Some people with these risks factors will never develop esophageal cancer and some people without any of these risk factors will nonetheless develop esophageal cancer.**

The main risk factors of esophageal squamous cell carcinoma are:

- **Tobacco use:** Smoking as well as chewing tobacco increases the risk of squamous cell carcinoma. The risk increases as the person smokes for a longer period or smokes multiple cigarettes a day.
- **Alcohol consumption:** The probability of getting squamous cell carcinoma is associated with the amount of alcohol consumed. Combining drinking of alcohol and smoking increases the risk much more than each of these two factors separately.
- **Low intake of fresh fruits and vegetables:** A higher risk of squamous cell carcinoma has been observed in people consuming insufficient amount of fruits and vegetables.
- **Drinking maté:** Maté is an infusion of a herb called yerba mate which is commonly consumed in South America. Heavy drinking (1 liter or more per day) of maté increases the risk of developing squamous cell carcinoma.
- **Betel quid chewing:** Betel quid is a mixture of plants that is chewed in many cultures in Southeast Asia. The leaves of the betel plant have a slightly stimulant effect but also increase the risk of esophageal cancer.
- **Certain medical conditions:**
  - o Achalasia increases the risk of developing squamous cell carcinoma. Achalasia is a disease in which the muscle which closes the lower esophagus cannot relax properly. Because swallowed food and liquids tend to collect in the esophagus, the lowest part dilates.
  - o Other rare diseases such as tylosis\* and Plummer-Vinson syndrome\* also increase the risk of squamous cell carcinoma of the esophagus.



The main risk factors\* of esophageal adenocarcinoma are:

- **Barrett's esophagus:** A Barrett's esophagus is the name of a situation where normal cells lining its inner part are replaced by cells resembling another type of cells normally found in the intestines. This change of one cell type that is normally found in a certain organ, into another cell type, is called metaplasia. This phenomenon is actually an adaptation of the lower esophagus to exposure to acid reflux\* from the stomach after a long period of time (years). Metaplastic cells are more likely than normal cells to turn into dysplastic and eventually even into cancer cells. Dysplasia is the disordered organization of cells, a condition that can evolve to cancer.

Risk factors for a Barrett's esophagus are:

- o Gastroesophageal reflux-disease: sometimes called acid reflux disease, it is a condition in which gastric acid regularly flows back into the esophagus. The

esophagus is damaged by this process. The most common symptom is heartburn. As a consequence, the inner lining can show metaplasia after a long time of acid reflux.

- Obesity increases the risk of Barrett's esophagus and esophageal adenocarcinoma by diverse mechanisms. This is partially explained by the higher risk of gastroesophageal reflux disease, but there is also a direct causal link. Acid reflux is more frequent and more severe in obese people, especially when the fat accumulates preferentially into the abdomen rather than into the thighs and hips.

Even if the majority of people with Barrett's esophagus will never develop esophageal cancer they should make medical appointments and undergo medical examinations on a regular basis. A gastro-enterologist should perform an endoscopy and take biopsies\* at regular intervals, to detect an evolution to dysplasia, or to esophageal cancer, as early as possible.

- Likewise, **tobacco use and alcohol consumption** can both increase the risk of adenocarcinoma, although the effect is smaller than in squamous cell carcinoma.

Other factors have been suspected to be associated with an increased risk of esophageal cancer like high intake of red meat or processed food, intake of high-temperature drinks, or exposure to certain chemicals. Others seem to have a protective effect, like infection with *Helicobacter pylori*\* in the stomach and long-term use of drugs from the group of Non-Steroidal Anti-Inflammatory Drugs (NSAID\*). However, the evidence is inconsistent and more research is needed.

## HOW IS ESOPHAGEAL CANCER DIAGNOSED?

Esophageal cancer can be suspected in different situations.

For people with Barrett's esophagus, regular screening should be performed to detect any evolution to adenocarcinoma as early as possible.

For others, some symptoms can possibly indicate the presence of an esophageal cancer.

- Difficulty in swallowing (dysphagia), hiccups, or food coming back up the esophagus.
- Unexplainable weight loss
- Pain or discomfort in the throat or in the back
- Hoarseness
- Long-lasting cough
- Vomiting, or coughing up blood

All these symptoms can be caused by other conditions and the doctor will gather information to see what could most likely explain the symptoms. When several symptoms occur at the same time, especially if they persist, further investigations should always be considered.

The diagnosis of esophageal cancer is based on the following examinations

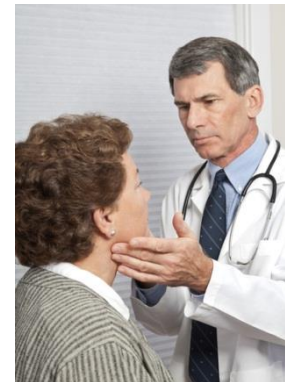
### 1. Clinical examination.

The doctor will ask about your symptoms and perform a clinical examination. This includes an examination of the abdomen and of the lymph nodes\* in the neck and the armpits.

### 2. Endoscopic examination.

During an endoscopic examination of the upper digestive tract or esophagogastroscope, the doctor passes a thin, flexible, lighted tube called an endoscope down the patient's throat. This enables the doctor to see the lining of the esophagus, stomach, and the first part of the small intestine. The doctor can also check the upper part of the trachea (airway). If abnormal areas are noted, biopsies\* (tissue samples) can be taken using instruments passed through the endoscope. These tissue samples are examined by a specialist in the laboratory (see histopathological\* examination).

During the endoscopy, an **endoscopic ultrasound\*** can be performed at the same time. An ultrasound probe is introduced down the throat into the esophagus. It provides images of different layers of the esophageal wall, as well as the nearby lymph nodes\* and other structures. This technique is used to see how far a cancer has spread in the esophageal wall, into nearby tissues or to nearby lymph nodes, which is very important to know in more detail and in advance for patients who will be operated. This reveals useful information for surgery and can also guide the doctor to remove a small sample (biopsy) of a suspicious lesion during the endoscopy. Performing an endoscopic ultrasound is, therefore, particularly useful before surgery.





### 3. Radiological examination.

To help with the diagnosis and to evaluate the extent of the tumor to plan the treatment, doctors will need to perform some radiological examinations. CT-scan\* of the chest and abdomen is usually performed. Barium swallow may also be performed to indicate precisely where the tumor is located in the esophagus. A barium swallow or barium meal involves taking X-ray\* pictures while the person drinks a special fluid. Because this fluid is very bright on the X-ray picture, the inner lining of the esophagus is clearly outlined on the X-ray. A PET-scan can be used to see how far the cancer has spread outside the esophagus. An endoscopy examining the airways (pharynx, larynx, trachea and bronchi) can also be performed.



### 4. Histopathological\* examination.

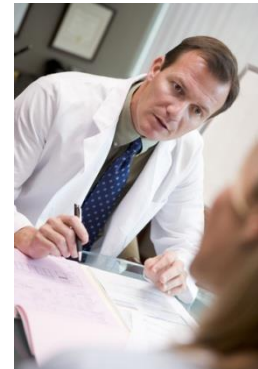
The biopsy\* specimen which is the tissue sample that has been taken during the endoscopy, will be examined in the laboratory by a pathologist\*. This is called a histopathological examination. Using the microscope and several other tests, the pathologist will confirm the diagnosis of cancer and will give more information on the characteristics of the cancer. This includes defining the histological type\*, being either squamous cell carcinoma if the tumor consists of flat cells lining the esophagus, or adenocarcinoma if it consists of cells that make and release mucus\* and other fluids.



When surgery is performed to remove a tumor, the tumor and the lymph nodes will also be examined in the lab. This is very important to confirm the results of the biopsy and to provide more information on the cancer.

## WHAT IS IT IMPORTANT TO KNOW TO GET THE OPTIMAL TREATMENT?

Doctors will need to consider many aspects of both the patient and the cancer in order to decide on the optimal treatment.



### Relevant information about the patient

- personal medical history
- results of the physical examination
- general well-being and fitness
- results of a blood examination, including a blood count to check for anemia\*, and liver and kidney function tests
- the results of endoscopy and a CT scan of chest and abdomen. In some patients an endoscopic ultrasound\* and/or a barium swallow will be performed.
- results of a preoperative evaluation. According to the patient's general health status this might include additional blood tests, an X-ray\* of the chest, an ECG\* or electrocardiogram, and a pulmonary function test.
- patient's preferences regarding treatment type

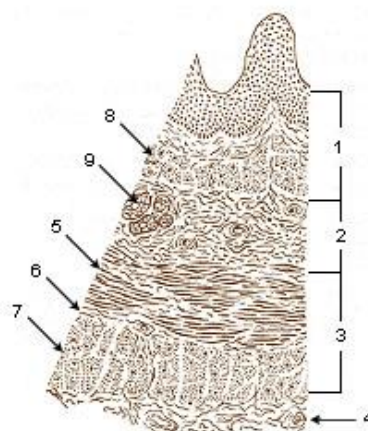
The results are important to decide whether the patient is fit enough to undergo surgery.

### Relevant information about the cancer

#### • Staging

Doctors use staging to assess the extent of the cancer (i.e. how far it has spread in the patient's body) and the prognosis\* of the patient. The TNM staging system is commonly used. The combination of T, size of the tumor and invasion of nearby tissue, N, involvement of lymph nodes\*, and M, metastasis\* or spread of the cancer to other organs of the body, will classify the cancer into one of the stages presented in the table.

To understand the definitions of the local extent of the tumor, it is important to know that the esophageal wall is built up by different layers, as illustrated in the picture below



Section of the esophageal wall. From the inside to the outside of the esophagus, the different layers are:

1: Mucosa\*, consisting of epithelium\*, lamina propria\* and muscularis mucosae\* (8). The mucosa or mucous membrane is the inner layer of the esophagus and it secretes several fluids.

2: Submucosa\*, containing the esophageal glands (9). The submucosa supports the mucosa and connects it with the underlying muscle layers. The glands produce a mucus and open upon the surface by a long duct. The mucous plays a role in lubricating and protecting the esophageal wall.

3: Muscularis propria, with 5, 6 and 7 being different muscle layers. The muscle layers contract in an alternating way in order to move on the food that passes through the esophagus.

4: Tunica adventitia. This outer layer consists of connective tissue and gives support to the esophagus.

Knowing the exact stage of the cancer is fundamental in order to make the right decision about the treatment. The lower the stage is, the better the prognosis\*. Staging is usually performed twice: after a clinical and radiological examination and after surgery. If surgery is performed, staging may also take into account the laboratory examination of the removed tumor.

The table below presents the different stages of esophageal cancer. The definitions may be technical so it is recommended to ask doctors for more detailed explanations.

Stage	Definition
Stage 0	<i>The tumor is called carcinoma in situ, meaning it only affects the epithelium*, or the histopathological* examination showed no cancer but does show high-grade dysplasia. Dysplasia is a disordered organization of cells lining the esophagus. There is no spread of the tumor to lymph nodes* or to other parts of the body.</i>
Stage I	<i>The tumor invades deeper in the esophageal wall. There is no spread of the tumor to lymph nodes, or to other parts of the body.</i>
Stage IA	<i>The tumor invades the mucosa* (T1a) or the submucosa* (T1b).</i>
Stage IB	<i>The tumor invades the muscularis propria (T2).</i>
Stage II	<i>The tumor invades the deepest layer of the esophageal wall, called tunica adventitia, or has affected 1 or 2 nearby lymph nodes. There is no spread to other parts of the body.</i>
Stage IIA	<i>The tumor invades the tunica adventitia (T3). There is no spread of the tumor to lymph nodes.</i>
Stage IIB	<i>The tumor invades the mucosa (T1a), submucosa (T1b) or muscularis propria (T2), and 1 or 2 nearby lymph nodes are affected.</i>
Stage III	<i>The tumor affects more than 2 lymph nodes, or has started invading nearby tissues. There is no spread to other parts of the body.</i>
Stage IIIA	<ul style="list-style-type: none"> <li>– <i>The tumor invades the pleura*, the pericardium* or the diaphragm* and there is no spread to lymph nodes or</i></li> <li>– <i>The tumor invades the tunica adventitia and 1 or 2 nearby lymph nodes are affected, or</i></li> <li>– <i>The tumor invades the mucosa, submucosa or muscularis propria and 3 to 6 regional lymph nodes are affected.</i></li> </ul>
Stage IIIB	<i>The tumor invades the tunica adventitia and 3 to 6 lymph nodes are affected.</i>
Stage IIIC	<ul style="list-style-type: none"> <li>– <i>The tumor invades the pleura*, the pericardium* or the diaphragm* and 1 to 6 lymph nodes are affected, or</i></li> <li>– <i>The tumor invades nearby tissues such as the aorta, a vertebra or the trachea (airway), regardless of the affection of lymph nodes, or</i></li> <li>– <i>More than 6 lymph nodes are affected, regardless of the local invasion of the tumor.</i></li> </ul>
Stage IV	<i>There is a spread to other parts of the body, regardless of the local invasion of the tumor and the extent to which the lymph nodes are affected.</i>

- **Resectability**

The surgeons will either judge the tumor as operable (or resectable), meaning that it is possible to remove the complete tumor in an operation, or as inoperable (or unresectable), meaning that this is not possible. A tumor can be unresectable because it has grown too far into nearby tissues or lymph nodes\*, because it is too close to major blood vessels, or because it has spread to distant parts of the body. There is no distinct dividing line between resectable and unresectable in terms of the TNM stage of the cancer, but earlier stage cancers are more likely to be resectable. The decision will also depend on whether the person is fit enough to undergo the operation.

- **Location of the tumor in the esophagus**

To make the best treatment choice it is important to know the location of the tumor. According to their vertical location in the esophagus, tumors are usually categorized as:

- cervical, which corresponds to the upper region, located in the neck;
- intrathoracic, which corresponds to the middle region, located in the chest;
- esophago-gastric junction, which corresponds to the lowest part, connecting to the stomach.

- **Results of the biopsy\***

The biopsy will be examined in the laboratory. This examination is called histopathology\*. The second histopathological examination involves the examination of the tumor and the lymph nodes\* after surgical removal. This is very important to confirm the results of the biopsy and to provide more information on the cancer. Results of the examination of the biopsy should include:

- **Histological type\***  
Histological type is based on the type of cells that compose the tumor. If the tumor consists of flat cells lining the esophagus, it is squamous cell carcinoma. If it consists of cells that make and release mucus\* and other fluids, it is an adenocarcinoma. If the pathologist\* defines the cancer as a small cell carcinoma, a very rare type of esophageal cancer, it will be treated accordingly. However, the information provided in this Guide for Patients does not apply to small cell carcinomas.
- **Grade**  
The grade is based on how different from normal esophageal cells tumor cells look and on how quickly they multiply. For esophageal cancer, the grade will be any value between one and four. The lower the grade, the better the prognosis\*.

Besides investigating the biopsy under the microscope, the pathologist\* will perform certain tests that give information about the genes of the tumor cells. These tests include fluorescent in situ hybridization (FISH\*) or immunohistochemistry\*.

- **HER2\*-status**  
This test should be done for adenocarcinoma of the lowest part of the esophagus, near the junction with the stomach. Using a FISH\*-test or immunohistochemistry, the pathologist investigates the genes of the cancer cells. Some cells have an amplification of a gene called HER2, meaning that there are too many copies of it in one of the cell's chromosomes\*. The HER2 gene is responsible for the production of a protein that may make a cell more malignant by influencing its growth and migration. Moreover, it is an important element in defining the treatment options. When there are too many copies of HER2 and too much content of the corresponding protein in the tumor cells, we speak of a HER2-positive cancer. Otherwise, the HER2 status is negative. HER2 positive cancers are aggressive in nature.

## WHAT ARE THE TREATMENT OPTIONS?

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Planning of the treatment involves an inter-disciplinary team of medical professionals. This usually implies a meeting of different specialists, called multidisciplinary opinion\* or tumor board review. In this meeting, the planning of treatment will be discussed according to the relevant information mentioned before.



The treatment will usually combine intervention methods that:

- Act on the cancer locally, such as surgery or radiotherapy\*
- Act on cancer cells all over the body by systemic therapy\* such as chemotherapy

The type and extent of the treatment will depend on the stage of the cancer, on the characteristics of the tumor and on the risks involved.

Treatments listed below have their benefits, their risks and their contraindications. It is recommended to ask oncologists about the expected benefits and risks of every treatment in order to be informed of the possible consequences. For some patients, several options are available and the choice should be discussed according to the balance between benefits and risks for the patient.

When a tumor is judged as resectable and the patient fit enough, surgery is the treatment of choice. This is in case of localized disease. Surgery is then the preferred option, but since surgery of the esophagus carries high risks, not all patients can be operated on. The tumor stage, location, histopathological\* type of the tumor (adenocarcinoma or squamous cell carcinoma) and the fitness of the patients strongly determinate the possibility of undergoing surgery successfully. The spread of the tumor to other organs (extensive disease) usually excludes surgery.

### Treatment plan for stage 0 to stage III adenocarcinoma

*The tumor is of the adenocarcinoma type and it is limited to the esophagus or has spread to adjacent structures. Regional lymph nodes\* may or may not be affected. There is no spread to other parts of the body.*

#### **1. The tumor is judged operable**

Surgery is the recommended treatment. The part of the esophagus containing the tumor will be removed.

For locally advanced stages (stage III) the treatment will be discussed in the multidisciplinary team\*. Depending on the extent and stage of the tumor, chemotherapy\* can be administered before and after the operation, or a combination of chemotherapy and radiotherapy\* can be given before the operation. This strategy aims to reduce the size of the tumor and to eliminate the cancer cells that will not be removed by the surgical intervention, therefore improving the results of the operation.

#### **Surgery**

Surgery is the treatment of choice in fit patients. When nearby lymph nodes\* are affected, surgery is still the best treatment. However, affected lymph nodes hamper the chance for cure of the patients and therefore a combined treatment including chemotherapy or chemotherapy with radiotherapy\* should be discussed in a multidisciplinary team\* if an involvement of lymph nodes is suspected in initial staging.

### Surgical procedures

The part of the esophagus containing the tumor will be removed during surgery. There are different ways or techniques to remove the tumor. It is not clear which type of surgery should be recommended. The decision on the technique will depend on the localization, on the extent of the tumor and on the expertise of the surgeon. In addition to the removal of the esophagus as described below, the surgeon will remove all nearby lymph nodes together with the esophagus. They will be examined by the pathologist\* to see if they contain cancer cells, which is important to define the stage. In most cases also a part of the stomach will be removed.



The esophagus and lymph nodes can be removed by making 2 incisions (neck and abdomen) or 3 incisions. When most of the esophagus is removed this means that the tumor is removed together with large margins of healthy tissue above and under the tumor. Afterwards the stomach will be lifted and connected to the upper part of the esophagus. In some cases, the surgeons can use part of the intestines to replace the esophagus.

It is not clear which type of surgery should be recommended and this will mainly depend on the experience of the surgeon.

Surgery of the esophagus carries high risk. The surgeons should be experienced with these types of procedures. The risks and side effects of surgery of the esophagus are presented later in this document. They should be discussed upfront with doctors.

### Adjuvant therapy

An adjuvant therapy is a therapy given in addition to the main treatment, which, in this case, is the removal of the tumor by surgery. Chemotherapy used before surgery and, if possible, after surgery is the standard treatment. The combination of both radiotherapy and chemotherapy before surgery is another option. The benefits and risks of the different strategies are explained below.

**Chemotherapy** is the use of drugs that aim to kill tumor cells or limit their growth. When it is administered before surgery, the intention is to reduce the size of the tumor and make its removal by surgery easier. This strategy is called preoperative or **neo-adjuvant chemotherapy**. It gives a benefit in all types of esophageal cancer, but the advantage is greatest in adenocarcinoma.

Patients who have adenocarcinoma located in the lowest part of the esophagus (near the stomach) can benefit from chemotherapy administered before and after surgery. Chemotherapy that is given both before and after surgery is called **perioperative chemotherapy**. It is currently recommended for patients with locally-advanced adenocarcinoma.

The drugs used to treat adenocarcinoma are cisplatin\*, 5-fluorouracil\* and possibly epirubicin\*. This depends on the decision of your doctor.

The most frequent side effects of chemotherapies are described further in the text. Side effects are usually reversible after treatment. Some strategies are available to prevent or relieve a certain range of these side effects. This should be discussed upfront with doctors.



Radiotherapy\* combined with chemotherapy administered before surgery (**preoperative chemoradiation**) is another treatment option. However, it is still unknown which patients benefit

from this intensive therapy. Chemoradiation\* is the combination of chemotherapy and radiotherapy within the same timeframe and following a specific schedule. Radiotherapy is the use of radiation, directed at the location of the tumor, to kill cancer cells. Recent research suggests that chemoradiation followed by surgery would increase the survival of patients, especially in patients with locally advanced adenocarcinoma. Unfortunately, the use of both radiotherapy and chemotherapy increase the risk of experiencing side effects. It has been shown that patients might be weakened before surgery and then might have a higher risk of severe complications after the operation. This is why not all patients should undergo preoperative chemoradiation and why a multidisciplinary team\* of physicians should discuss what may be the best therapy for the individual patient.

Side effects of chemoradiation include those of chemotherapy and those of radiotherapy. The drugs that are mostly used are cisplatin\* and 5-fluorouracil\*, but other drugs can be used at the discretion of your doctor. The most frequent side effects of chemotherapy and radiotherapy are described further in the text. They are usually reversible after treatment. Some strategies are available to prevent or relieve a certain range of these side effects. This should be discussed upfront with doctors.

Chemotherapy and chemoradiation can also be administered after surgery. This is called postoperative or adjuvant treatment. However, today it is still not clear how much benefit chemotherapy and chemoradiation after surgery would give, and the side effects of the treatment can be difficult to cope with. The only exception where postoperative chemotherapy or chemoradiation show a clear benefit is for people with an adenocarcinoma of the lowest part of the esophagus after limited surgery. Limited surgery means that during the operation, only a limited number of lymph nodes\* were removed together with the affected part of the esophagus.

## **2. The tumor is judged inoperable**

When a tumor is judged to be inoperable or the patient is not fit enough to undergo surgery, the combination of chemotherapy\* and radiotherapy\* (chemoradiation) is preferred since it has been proven to be more effective than radiotherapy alone. The drugs usually administered are cisplatin\* and 5-fluorouracil\*, but other drugs can be used at the decision of your doctor. Chemotherapy alone can also be considered. The treatment choice will always be discussed in a multidisciplinary team\*.

The chemoradiation or chemotherapy can be given with the intent to cure the cancer, or to relieve symptoms, depending on the extent of the tumor.

The most frequent side effects of chemotherapy and radiotherapy are described further in the text. They are usually reversible after treatment. Some strategies are available to prevent or relieve a certain range of these side effects. This should be discussed upfront with doctors.

## **Treatment plan for stage 0 to stage III squamous cell carcinoma**

*The tumor is of the squamous cell type and it is limited to the esophagus or has spread to adjacent structures. Regional lymph nodes\* may or may not be affected. There is no spread to other parts of the body.*

### **1. The tumor is judged operable**

Surgery is the recommended treatment. The part of the esophagus containing the tumor will be removed. The type of surgery will depend on the extent of the tumor.

In tumors that invaded the deepest layer of the esophageal wall or adjacent structures, chemotherapy alone or a combination of chemotherapy\* and radiotherapy\* (chemoradiation)

administered before the operation can improve the results of the operation. When the tumor responds well to the chemotherapy or the chemoradiation, surgery can be postponed or even become redundant. These treatment options will be discussed in a multidisciplinary team. After surgery an additional series of chemoradiation might be discussed in case the tumor could not be completely resected.

## Surgery

Surgery is the treatment of choice for early cancer in fit patients. When nearby lymph nodes\* are affected, surgery is still the best treatment. However, affected lymph nodes hamper the chance for cure of the patients and therefore a combined treatment including chemotherapy or chemotherapy with radiotherapy should be discussed in a multidisciplinary team\* if an involvement of lymph nodes is suspected in initial staging.

## Procedures of surgery

There are different ways or techniques to remove the tumor. The decision on the technique will depend on the localization, on the extent of the tumor and on the expertise of the surgeon. In addition to the removal of the esophagus (as described below), the surgeon will remove all nearby lymph nodes together with the esophagus. They will be examined by the pathologist\* to see if they contain cancer cells.

- **Endoscopic\* resection for squamous cell carcinoma limited to the mucosa\***

Endoscopic resection is the removal of a part of the esophagus through endoscopy. For this operation, the doctor passes a thin, flexible, lighted tube called an endoscope down in the patient's throat. The endoscope is combined with a surgical instrument that allows performing a resection of the tumor. It is recommended for squamous cell carcinoma limited to the mucosa, and if it can be done in specialized centers where the surgeons or gastroenterologists\* have experience with this kind of operation. Overall, this technique allows the patient's esophagus to be saved.

- **Removal of a part of or the entire esophagus for squamous cell carcinoma extended to the deepest layer of the esophageal wall or adjacent structures, with or without invasion of regional lymph nodes\***

The type of surgery depends on the location of the tumor. In addition to surgery, in tumors invading the deepest layer of the esophageal wall or adjacent structures, a combination of chemotherapy\* and radiotherapy\* administered before the operation can reduce the size of the tumor and therefore improve the results of the operation.



- **Squamous cell carcinoma of the upper part of the esophagus (cervical)**

The esophagus and lymph nodes may be removed by using 2 incisions (neck and abdomen) or 3 incisions. It is not clear which type of surgery should be recommended and this will mainly depend on the experience of the surgeon.

- **Squamous cell carcinoma of the middle part of the esophagus (intrathoracic)**

When a squamous cell carcinoma is located in the middle region of the esophagus, transthoracic esophagectomy is recommended. The surgeons will make two incisions, one in the abdomen and another one in the chest. Most of the esophagus is removed meaning that the tumor is removed together with large margins of healthy tissue above and under the tumor. Afterwards the stomach will be brought up and



connected to the upper part of the esophagus. When the stomach cannot be used, the surgeons use part of the intestine to replace the esophagus.

- **Squamous cell carcinoma of the lowest part of the esophagus (esophago-gastric junction)**

When the tumor is located in the lowest part of the esophagus, near the stomach, a part of the stomach will be removed as well. The remaining part of the stomach will be connected to the upper part of the esophagus. Two incisions are usually done, one in the abdomen and one in the neck, but none in the chest. Some techniques will involve three incisions, in the abdomen, chest and neck.

Surgery of the esophagus carries high risk and is not without side effects. The surgeons should be experienced with this type of procedures. The risks and side effects of surgery on the esophagus are presented later in this document. They should be discussed upfront with doctors.

### **Adjuvant therapy**

An adjuvant therapy is a therapy given in addition to the main stage of the treatment which is in this case the removal of the tumor by surgery.

The decision to give chemotherapy and sometimes radiotherapy\* before surgery depends on the extent and stage of the tumor.

The decision to give chemotherapy combined with radiotherapy after surgery depends on whether the tumor has been completely resected by the surgeon.

**Chemoradiation\*** is the combination of chemotherapy and radiation therapy within the same timeframe and following a specific schedule. Chemotherapy is the use of drugs that aim to kill tumor cells or limit their growth. Radiotherapy aims to kill tumor cells using radiation, directed specifically to the area of the cancer.

The effect of chemoradiation administered before surgery is still under study and is not yet proven for all patients. Recent research suggested that chemoradiation followed by surgery could increase the survival of patients with a squamous cell carcinoma extended to the deepest layer of the esophageal wall or adjacent structures. Unfortunately, the use of both radiotherapy and chemotherapy increases the risk of experiencing side effects. It has been shown that patients might be weakened before surgery and then might be at a higher risk of severe complications after the operation. This is why it is not yet clear which patients would benefit from preoperative chemoradiation. It is, however, recommended in all patients with a tumor extending into the deepest layer of the esophageal wall or adjacent structures.

Side effects of chemoradiation include those of chemotherapy and those of radiotherapy. The most frequent side effects of chemotherapy and radiotherapy are described later in the text (see *'Possible side effects of the therapies used to treat esophageal cancers'*). They are usually reversible after treatment. Some strategies are available to prevent or relieve a certain range of these side effects. This should be discussed upfront with doctors.

When the doctors notice that the tumor responds well to the chemoradiation, they might as well decide to continue with this treatment and to postpone surgery. A response of the tumor means the size of the tumor is reduced because of the treatment. Response is evaluated by the way the patient feels, by an endoscopy\* (with new biopsies\*) and by imaging techniques. These can be an esophagogram\*, a CT-scan\* or a PET-scan\*. In case of a good response, the doctors may increase the dose of radiation. Studies have shown that by doing this, the survival of patients is the same as with surgery. However, there is a higher probability that the tumor will recur at its original site in the

esophagus. Therefore close surveillance of the patient by an experienced multidisciplinary team\* and early surgery in case of tumor progression is very important.

In some cases, surgery will not be necessary. The treatment is then called definitive chemoradiation. This strategy is particularly recommended in patients with a tumor in the upper, cervical part of the esophagus, since these tumors are hard to remove by surgery.

After surgery, the part of the esophagus that is removed will be examined by a pathologist\* in the laboratory. This is called the histopathological\* examination. The pathologist will check if the margins of the resected part are tumor-free and thus if the complete tumor has been removed. If cancer cells are found in the margins of the resected part, this means a part of the tumor is left behind. In that case additional chemoradiation might be administered to eliminate the cancer cells that are still in the body. This is called post-operative or adjuvant treatment.

However, today it is not clear yet how much benefit chemoradiation after surgery would give.

## **2. The tumor is judged inoperable**

For patients not fit enough or unwilling to undergo surgery, chemoradiation\* has a better effect than radiotherapy\* alone. The treatment will always be discussed in a multidisciplinary team\*. The drugs that are usually administered are cisplatin\* and 5-fluorouracil\*, but other drugs can be used at the decision of your doctor. The dose of radiation that is regarded as standard treatment can be up to or above 60 Gy and higher levels usually recommended. Gy stands for Gray and is a unit for the dose of radiation that is administered during radiotherapy. The chemoradiation can be given with the intent to cure the cancer, to relieve symptoms, or both, depending on the extent of the tumor.

## **Treatment plan for metastatic\* disease (stage IV)**

*The tumor is either of the squamous cell or of the adenocarcinoma type and it has spread to other parts of the body like to the lungs or to the liver, regardless of the local invasion of the tumor and the affection of lymph nodes\*.*

Patients with metastatic esophageal cancer can be considered for different treatment options to relieve their symptoms. The choice made will depend on their specific situation.

### **Local treatment**

**Brachytherapy** is a type of radiotherapy\* in which radioactive material is placed directly into or near the tumor. Because of the close location to the tumor and the short distance the radiation has to travel, higher doses of radiation can be administered than in external radiotherapy, which uses radiations coming from outside the body and directed to the area of the tumor. This strategy can relieve discomfort and difficulties swallowing in patients with metastatic\* esophageal cancer. It has been proven to have a better long term effect and fewer unwanted effects than the placement of a **stent**. A stent is a metal tube that is placed inside the esophagus to stop it being blocked by the tumor as it grows and it thus allow the passage of food through the esophagus. Side effects of brachytherapy are a temporary sore throat and sickness. With a stent, there is a risk that the tumor may grow over one end of the stent, after some time, and block the esophagus again.

### **Systemic therapy\***

A systemic therapy is a therapy that aims to act on cancer cells found anywhere in the body. Chemotherapy\* is the main type of systemic therapy. This is in contrast to local therapy such as surgery or radiotherapy\* that acts on cancer cells within a defined area.

Chemotherapy can help to reduce symptoms and should be considered particularly for patients who are fit and have good general health. Classically, cisplatin\* and 5-fluorouracil\* are used. However, some newer drugs from the same medication classes seem to offer higher efficacy and improved quality of life.

Patients with adenocarcinoma of the lowest part of the esophagus should be screened for HER2\* status. When there are too many copies of HER2-gene or too much protein of the corresponding HER2-protein, we speak about a HER2-positive cancer. In case of a HER2 positive cancer, a drug called trastuzumab\* could be added to the chemotherapy. Trastuzumab is a drug that specifically targets the HER2 protein. This type of treatment is called a targeted therapy\*.

## WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENT?

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### Risks and side effects of surgery

Removal of the esophagus is a high-risk surgical procedure. There are several risks and it can cause unwanted health problems, called complications. Complications can usually be treated, but are sometimes difficult to treat and can even be fatal.

Some risks are shared by all surgical interventions performed under general anaesthesia\*. These complications are infrequent and include deep vein thrombosis\*, heart or breathing problems, bleeding, infection, or reaction to the anaesthesia. Although there are risks, doctors will take the most appropriate steps to minimize them.

The joining of the stomach and the remaining part of the esophagus is called anastomosis. This anastomosis can sometimes leak after surgery, or provoke an infection in the chest. After a while, narrowing of the esophagus due to scar formation can cause difficulties in swallowing. During endoscopy\*, this narrowing can be dilated again, alleviating the problem.

In some patients the stomach takes longer to empty than before, which can cause nausea and vomiting. Others suffer from heartburn, because the muscle that separates the esophagus from the stomach has been removed. Effective medications exist to relieve these symptoms. A nutritionist\* or a dietician can give advice and help patients to start eating again and gradually adapt the food and drinks according to the healing process of the esophagus.

### Risks and side effects of chemotherapy\*

The main side-effects of chemotherapy are:

- hair loss
- nausea and vomiting
- diarrhea
- a sore mouth or mouth ulcers
- low blood cell counts. A decrease in white blood cells will increase the risk of getting infections and make it harder to fight them. A decrease in red blood cells\* leads to anemia\*, which can cause tiredness and breathlessness. A decrease in blood platelets\* can make people more sensitive to bruising and bleeding (e.g. nose bleeds or bleeding gums).

Apart from these, each drug can also give different unwanted effects. The most common ones are listed below, although not everyone will have side effects, or get them to the same extent.

- 5-fluorouracil\* can cause fatigue which can last for a few months after treatment.
- Cisplatin\* may lead to hearing loss, and to kidney damage. The kidney function is examined in the blood before starting the treatment. To prevent damage it is very important to drink a lot of water during the treatment.
- Epirubicin\* rarely causes damage to the heart muscle, although usually only when used for many months or in people with heart problems before treatment. If you have heart problems, your doctor will arrange a scan before treatment to see if your heart is strong enough for this treatment. It can make the skin more sensitive to sunlight and cause reddening in areas where the patient has had radiotherapy\* in the past. The urine may turn

red or pink for a few days after treatment. This is not blood and is only due to the color of the medication.

### **Risks and side effects of chemoradiation\***

The side effects of chemoradiation are equal to those of chemotherapy\* (as mentioned previously) and those of radiotherapy. The main side effects of radiotherapy delivered to the chest and/or to the stomach are sickness and a very sore throat. Because eating can be difficult, some patients temporarily lose weight or might need extra intravenous\* fluid.

### **Risks and side effects of targeted therapy\***

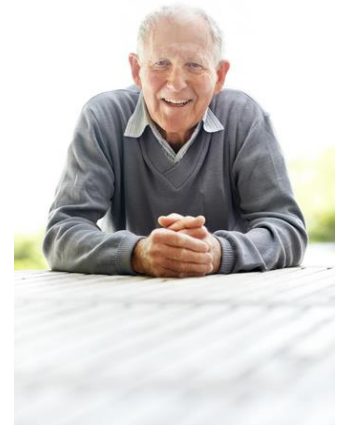
The most common side effects of trastuzumab\* are fatigue, diarrhea and a reaction to the drugs including chills, fever, sickness, wheezing, headache, and faintness. However, this reaction usually declines as treatment proceeds.

## WHAT HAPPENS AFTER TREATMENT?

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It is not unusual to experience treatment-related symptoms once treatment is over.

- It is not rare to experience anxiety, problems sleeping, or depression in the post-treatment phase; patients suffering from these symptoms may benefit from psychological support.
- Memory deficiencies and difficulty concentrating are not uncommon side effects of chemotherapy\* and are generally reversible within a few months.
- Swallowing can be painful for a while, especially with solid food. A nutritionist\* or a dietician can guide the patient in starting to eat again and adapt the diet according to the healing process of the esophagus.



### Follow-up\* with doctors

After the treatment has been completed, doctors propose a follow-up program consisting of consultations on a regular basis and aiming to:

- evaluate adverse effects of the treatment and treat them
- provide psychological support and information to enhance returning to normal life
- detect possible recurrence\* as soon as possible

There is no standard frequency or interval of follow-up visits that is advised.

Only when the chemoradiation\* was the only treatment of locally advanced squamous cell carcinoma, i.e. when no surgery was performed, a strict surveillance should be maintained. This is necessary to detect any growth or extension of the tumor (called progression) as early as possible and to proceed to surgery.

Follow-up visits with the oncologist should include

- History-taking, eliciting of symptoms, and clinical examination. The doctor or the dietician will also focus on diet and possible nutritional problems.
- In some cases the doctor might ask for a new endoscopy\* with a possible biopsy\*, or for imaging techniques as an esophagogram\*, a CT-scan\*, or a PET-scan\*.

### Return to normal life

It can be hard to live with the idea that the cancer can come back. Based on what is known today, no specific way of decreasing the risk of recurrence\* after completion of treatment can be recommended. Because of the cancer itself and because of treatment, returning to normal life may not be easy for some people. Questions related to body image, fatigue, work, emotions or lifestyle may arise. Discussing these questions with relatives, friends, or doctors may be helpful. Some people may also want to find support from ex-patients' groups or telephone information lines.

## **What if the cancer comes back?**

If the cancer comes back, it is called a recurrence\*. The treatment depends on the place and the extent of the recurrence, and on the treatments that have been given before. The cancer can reappear in the esophagus, or in another part of the body.

If the cancer comes back in the esophagus, this type of recurrence is often treated by removing the esophagus. If the patient is unable to have surgery due to other health problems, the cancer may be treated with chemotherapy, radiation, or both.

If cancer recurs locally after surgery, radiation and/or chemotherapy may be used. If radiation were given before, more radiation is rarely an option. If chemotherapy was given before, it is usually still possible to give more chemotherapy. Sometimes the same drugs that were used before are given again, but often other drugs are used.

Esophageal cancer that recurs in other organs or tissue\* should be treated as mentioned before in the part titled 'Treatment plan for metastatic\* disease (stage IV)'.

## DEFINITIONS OF DIFFICULT WORDS

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### **5- fluorouracil**

A drug used to treat symptoms of cancer of the colon, breast, stomach, and pancreas. It is also used in a cream form to treat certain skin conditions. 5-fluorouracil stops cells from making DNA and it may kill cancer cells. It is a type of antimetabolite. Also called 5-FU and fluorouracil.

### **Anemia**

Condition characterized by the shortage of red blood cells\* or hemoglobin, the iron that contains the hemoglobin carries oxygen from the lungs to the whole body, this process is diminished in this condition.

### **Anaesthesia**

Reversible state of loss of awareness in which the patient feels no pain, has no normal reflexes, and responds less to stress. It is induced artificially by the employment of certain substances known as anesthetics. It can be complete or partial and allows patients to undergo surgery.

### **Biopsy**

The removal of cells or tissue\* for examination by a pathologist\*. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy, in which only a sample of tissue is removed; (2) excisional biopsy, in which an entire lump or suspicious area is removed; and (3) needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

### **Blood platelet**

Small cell fragments that play a fundamental role in the formation of blood clots. Patients with a low platelet count are at risk of severe bleeding. Patients with a high count are at risk of thrombosis, the formation of blood clots that can block blood vessels and result in stroke or other severe conditions, and can also be at risk of severe bleeding because of platelet dysfunction.

### **Chemoradiation**

Treatment that combines chemotherapy\* with radiation therapy. Also called chemoradiotherapy.

### **Chemotherapy**

A type of cancer treatment using drugs that kill cancer cells and/or limit their growth. These drugs are usually administered to the patient by slow infusion into a vein but can also be administered orally, by direct infusion to the limb or by infusion to the liver, according to cancer location.

### **Chromosome**

An organized structure which encodes genes which are the body's code for characteristics such as hair color or gender. Human cells have 23 pairs of chromosomes (total of 46 chromosomes). Cancer or leukemia cells often have a chromosomal abnormality which is a change to their chromosomes, such as a chromosomal duplication or an extra chromosome (47 chromosomes) or have a chromosomal deletion or a loss of a chromosome (45 chromosomes). A chromosomal or genetic inversion is when no extra chromosomes are added or deleted, but instead a portion is backwards. In the word 'bdrawkcas', the middle has been inverted.



### **Cisplatin**

A drug used to treat many types of cancer. Cisplatin contains the metal platinum. It kills cancer cells by damaging their DNA and stopping them from dividing. Cisplatin is a type of alkylating agent.

### **CT-scan**

A form of radiography in which body organs are scanned with X-rays\* and the results are synthesized by a computer to generate images of parts of the body.

### **Deep vein thrombosis**

The formation of a blood clot in a deep vein of the leg or lower pelvis. Symptoms may include pain, swelling, warmth, and redness in the affected area. Also called DVT.

### **Diaphragm**

The thin muscle below the lungs and heart that separates the chest from the abdomen.

### **ECG/ electrocardiogram**

A line graph that shows changes in the electrical activity of the heart over time. It is made by an instrument called an electrocardiograph. The graph can show that there are abnormal conditions, such as blocked arteries, changes in electrolytes (particles with electrical charges), and changes in the way electrical currents pass through the heart tissue. Also called ECG and EKG.

### **Endoscopy/endoscopic**

A medical procedure where a doctor puts a tube-like instrument into the body to look inside. There are many types of endoscopy, each of which is designed for looking at a certain part of the body.

### **Endoscopic ultrasound**

A procedure in which an endoscope is inserted into the body. An endoscope is a thin, tube-like instrument that has a light and a lens for viewing. A probe at the end of the endoscope is used to bounce high-energy sound waves (ultrasound) off internal organs to make a picture (sonogram). Also called endosonography and EUS.

### **Epirubicin**

A drug used together with other drugs to treat early breast cancer that has spread to lymph nodes\*. It is also being studied in the treatment of other types of cancer. Epirubicin is a type of anthracycline antibiotic. Also called Ellence and epirubicin hydrochloride.

### **Epithelium**

The term "epithelium" refers to cells that line hollow organs and glands and those that make up the outer surface of the body. Epithelial cells help to protect or enclose organs. Most produce mucus\* or other secretions.

### **Esophagogram**

A series of x-ray pictures of the esophagus taken after a patient drinks a liquid containing barium sulfate (a form of the silver-white metallic element barium). The barium sulfate coats and outlines the inner wall of the esophagus so that it can be seen on the x-ray pictures. Also called contrast esophagram.

### **FISH/Fluorescence in situ hybridization**

**Esophageal cancer: a guide for patients - Information based on ESMO Clinical Practice Guidelines - v.2012.1** Page 24

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A technique used by pathologists\* to identify changes to genes and chromosomes\*. Unique changes to genes or chromosomes can be detected by FISH and help a pathologist know what type of leukemia a patient has.

### **Follow-up**

Monitoring a person's health over time after treatment. This includes keeping track of the health of people who participate in a clinical study or clinical trial for a period of time, both during the study and after the study ends.

### **Gastroenterologist**

A doctor who specializes in diagnosing and treating disorders of the digestive system.

### **Gastroesophageal reflux**

The backward flow of stomach acid contents into the esophagus (the tube that connects the mouth to the stomach). Also called esophageal reflux, gastric reflux or acid reflux.

### **Helicobacter pylori**

A type of bacterium that causes inflammation and ulcers in the stomach or small intestine. People with *Helicobacter pylori* infections may be more likely to develop cancer in the stomach, including MALT (mucosa-associated lymphoid tissue) lymphoma. Also called *H. pylori*.

### **HER2**

A protein involved in normal cell growth. It is found in some types of cancer cells, including breast and ovarian. Cancer cells removed from the body may be tested for the presence of HER2/neu to help decide on the best type of treatment. HER2/neu is a type of receptor tyrosine kinase. Also called c-erbB-2, human EGF receptor 2, and human epidermal growth factor receptor 2.

### **Histological type**

The category in which a tumor is grouped, considering the characteristics of its cells and other structures under the microscope.

### **Histopathology**

The study of diseased cells and tissue\* using a microscope.

### **Immunohistochemistry**

Immunohistochemistry or IHC refers to the process of detecting antigens (e.g., proteins) in cells of a tissue\* section by exploiting the principle of antibodies binding specifically to antigens in biological tissue. These antigens are visualized by a marker such as fluorescent dye, enzyme, or colloidal gold. Immunohistochemical staining is widely used in the diagnosis of abnormal cells such as those found in cancerous tumors.

### **Intravenous**

Into or within a vein. Intravenous usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein. Also called IV.

### **Lamina propria**

The lamina propria is a thin layer of loose connective tissue\* which lies beneath the epithelium\* and together with the epithelium constitutes the mucosa\*. The term mucosa or mucous membrane always refers to the combination of the epithelium plus the lamina propria.

### **Lymph node**

A rounded mass of lymphatic tissue\* that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph and they store lymphocytes. They are located along lymphatic vessels. Also called lymph gland.

### **Metastasis/metastase(s)/metastatic**

The spread of cancer from one part of the body to another. A tumor formed by cells that have spread is called a metastatic tumor or a metastasis. The metastatic tumor contains cells that are like those in the original tumor.

### **Mucosa**

The moist, inner lining of some organs and body cavities. Glands in the mucosa make mucus\*. Also called mucus membrane.

### **Mucus**

Mucus is a slick substance secreted by the mucous membranes that line many of the body's inner surfaces. It consists of proteins, antimicrobial enzymes, antibodies, and salt. Mucus serves to protect cells from the epithelium\* in the respiratory, gastrointestinal, urinary, genital, visual, and auditory systems.

### **Multidisciplinary opinion**

A treatment planning approach in which a number of doctors who are experts in different areas (disciplines) review and discuss the medical condition and treatment options of a patient. In cancer treatment, a multidisciplinary opinion may include that of a medical oncologist (who provides cancer treatment with drugs), a surgical oncologist (who provides cancer treatment with surgery), and a radiation\* oncologist (who provides cancer treatment with radiation\*). Also called tumor board review.

### **Muscularis Mucosae**

Thin, deep layer of smooth muscle fibers in some mucous membranes (mucosa), as well as in the digestive tract. Muscularis mucosae separates the mucous membranes from a deeper layer of tissue called submucosa.

### **Non-Steroidal Anti-Inflammatory Drugs (NSAID)**

A drug that decreases fever, swelling, pain, and redness. Also called NSAID.

### **Nutritionist**

A nutritionist is a health professional who advises on matters of food and nutrition impacts on health. Some use the terms "dietitian" and "nutritionist" as more or less interchangeably. However, there are important differences between countries regarding the training needed to be recognized as a nutritionist or as a dietitian. In some countries, any person may call themselves a nutrition expert even if they are wholly self-taught.

### **Pathologist**

A doctor specialized in histopathology\* which is the study of diseased cells and tissues using a microscope.

### **Pericardium**

The pericardium is a double-walled sac that surrounds the heart and the roots of the great blood vessels. It has several functions. It keeps the heart contained in the chest cavity and also prevents the

heart from overexpanding when blood volume increases. Within the pericardium lies the pericardial cavity. This cavity is filled with pericardial fluid which reduces friction between the pericardial membranes.

### **PET-scan**

A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is used. Because cancer cells often use more glucose than normal cells, the pictures can be used to find cancer cells in the body. Also called positron emission tomography scan.

### **Pleura**

A thin layer of tissue\* that covers the lungs and lines the interior wall of the chest cavity. It protects and cushions the lungs. This tissue secretes a small amount of fluid that acts as a lubricant, allowing the lungs to move smoothly in the chest cavity while breathing.

### **Plummer-Vinson Syndrome**

A disorder marked by anemia caused by iron deficiency, and a web-like growth of membranes in the throat that makes swallowing difficult. Having Plummer-Vinson syndrome may increase the risk of developing esophageal cancer. Also called Paterson-Kelly syndrome and sideropenic dysphagia.

### **Prognosis**

The likely outcome or course of a disease; the chance of recovery or recurrence\*.

### **Radiotherapy**

A therapy in which radiation is used in the treatment of cancer always oriented to the specific area of the cancer.

### **Recurrence**

Cancer or disease (usually auto-immune) that has come back, usually after a period of time during which the cancer or disease was not present or could not be detected. This may happen at the same location as the original (primary) tumor or to another location in the body. Also called recurrent cancer or disease.

### **Red blood cells**

The most common type of blood cell. It is the substance that makes the blood appear red. The main function is the transport of oxygen.

### **Risk factor**

Something that increases the chance of developing a disease. Some examples of risk factors for cancer are age, a family history of certain cancers, use of tobacco products, being exposed to radiation or certain chemicals, infection with certain viruses or bacteria, and certain genetic changes.

### **Submucosa**

In the gastrointestinal tract, the submucosa is the layer of dense irregular connective tissue\* or loose connective tissue that supports the mucosa\*, as well as joins the mucosa to the bulk of underlying smooth muscle (fibers running circularly within layers of longitudinal muscle).

### **Systemic therapy**

Treatment using substances that travel through the bloodstream, reaching and affecting cells all over the body. Chemotherapy and immunotherapy are examples of systemic therapy.

**Esophageal cancer: a guide for patients - Information based on ESMO Clinical Practice Guidelines - v.2012.1** Page 27

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**Targeted therapy**

A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to identify and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

**Tissue**

A group or layer of cells that work together to perform a specific function.

**Trastuzumab**

Trastuzumab is a monoclonal antibody. Trastuzumab has been designed to attach to HER2\*. By attaching to HER2, trastuzumab activates cells of the immune system, which then kill the tumour cells. Trastuzumab also stops HER2 producing signals that cause the tumour cells to grow. About a quarter of breast cancers and a fifth of gastric cancers overexpress HER2.

**Tylosis**

An inherited disorder marked by hyperkeratosis (callosities) of the palms and soles and abnormal patches of white tissue in the mouth, known as oral leukoplakia.

**X-ray**

X-rays are a form of radiation used to take images of the inside of objects. In medicine, X-rays are commonly used to take images of the inside of the body.

The ESMO / Anticancer Fund 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.

These guides are produced by the Anticancer Fund in close collaboration with the ESMO Guidelines Working Group and the ESMO Cancer Patient Working Group.

For more information please visit [www.esmo.org](http://www.esmo.org) and [www.anticancerfund.org](http://www.anticancerfund.org)

