

PANCREATIC CANCER: A GUIDE FOR PATIENTS

PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by Reliable Cancer Therapies (RCT) as a service to patients, to help patients and their relatives better understand the nature of pancreatic cancer and appreciate the best treatment choices available according to the subtype of pancreatic cancer. We recommend that patients ask their doctors about 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 pancreatic 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 patient representatives from ESMO's Cancer Patient Working Group.

More information about Reliable Cancer Therapies: www.reliablecancertherapies.com

More information about the European Society for Medical Oncology: www.esmo.org

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

Table of contents

Definition of pancreatic cancer	3
Is pancreatic cancer frequent?.....	4
What causes pancreatic cancer?.....	5
How is pancreatic cancer diagnosed?	6
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 therapies?	19
What happens after the treatment?	20
Definitions of medical terms	22

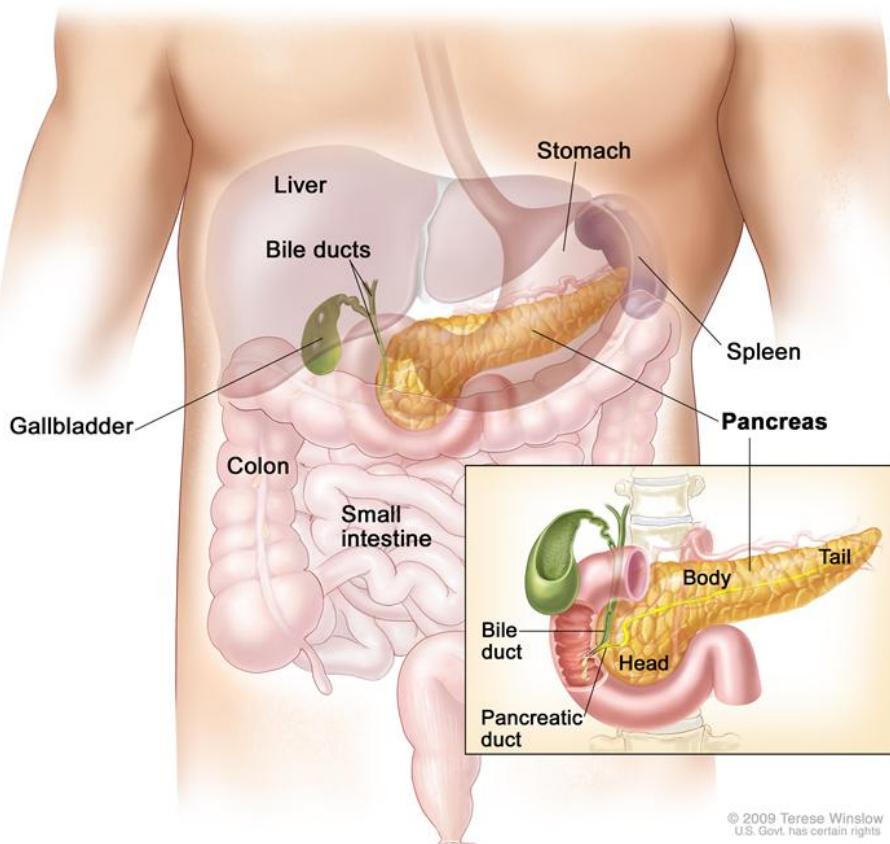
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DEFINITION OF PANCREATIC CANCER

Pancreatic cancer is a disease in which abnormal cells appear in the tissue of the pancreas. The pancreas is an organ located in the abdomen behind the stomach. It produces both digestive enzymes* and insulin*. The pancreas is made up of two different kinds of tissue with different functions: the exocrine* pancreas, which secretes enzymes into the digestive tract, which help to break down fats and proteins, and the endocrine* pancreas, which secretes glucagon* and insulin into the bloodstream in order to control blood sugar levels. In more than 80% of the cases, pancreatic cancer develops in the exocrine pancreas. About 75% of all exocrine pancreatic cancers occur within the head or neck of the pancreas, 15 to 20% in the body and 5 to 10% in the tail of the pancreas.



Anatomy of the pancreas. The pancreas has three parts: head, body and tail. It is found in the abdomen near the stomach, intestines and other organs.

Important note regarding other tumors of the pancreas

This guide for patients provides information about cancer of the exocrine* pancreas, the most common type of cancer of the pancreas, also known as pancreatic adenocarcinoma. Acinar cell carcinomas and pancreatoblastomas are other tumor types occurring in the exocrine part of the pancreas, but they are very rare, and information in this guide refers to pancreatic adenocarcinoma only. Cystic tumors of the pancreas such as intraductal papillary mucinous neoplasms (IPMNs) are also not covered by this guide.



Another type of tumor of the pancreas develops in the endocrine* pancreas. These tumors are rare and are called neuroendocrine tumors* (NETs). Diagnosis and treatment of these tumors is different from the diagnosis and treatment of the exocrine tumors described in this guide.

IS PANCREATIC CANCER FREQUENT?

In Europe, pancreatic cancer is the seventh most frequent cancer. In the European Union, 11.6 men out of 100,000 are diagnosed with pancreatic cancer each year, this frequency ranges between 4.7 (Cyprus) to 17.2 (Hungary), being the cause of death of approximately 35,000 men every year. In women it affects 8.1 out of 100,000 women ranging from 2.1 (Cyprus) to 11.4 (Finland). It is also the cause of death of 35,000 women every year. The frequency of new diagnosed cases increases with age, and most of the cases are diagnosed above the age of 65.

Because the disease is often goes unnoticed for a long time, the diagnosis is often made when the tumor has spread to other organs. It is the fifth leading cause of cancer-related deaths.

WHAT CAUSES PANCREATIC CANCER?

Today, it is not clear why pancreatic cancer occurs. Most pancreatic cancers (90%) are considered not to be associated to any risk factor, nevertheless some risk factors* for others 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 pancreatic cancer and some people without any of these risk factors will develop it.**

The main risk factors of pancreatic cancer identified so far are:

- **Genes:**
 - o Certain genetic mutations* are known to be related to pancreatic cancer. Most pancreatic cancers have somatic mutations in genes KRAS (80%), p53 (50%) and p16, which are associated with the control of tumor growth. Other genes that show alterations or mutations associated to pancreatic cancer are CDKN2 (90%) and DPC4/Smad4 (50%). BRCA2 is another gene whose mutation results in hereditary breast and ovarian cancer syndromes. It has also been shown to be involved in some pancreatic cancers.
 - o Rare inherited genetic conditions such as hereditary pancreatitis, Peutz-Jeghers syndrome*, Familial Atypical Multiple Mole Melanoma syndrome*, hereditary breast and ovarian cancer syndrome and hereditary non polyposis colorectal cancer syndrome (HNPCC or Lynch syndrome) are associated with an increased risk of developing pancreatic cancer. The term hereditary refers to genetic traits passed down from generation to generation by family members. Having a first- (parents or siblings) or a second-degree relative (uncles, aunts or cousins) affected by pancreatic cancer increases the risk of developing it too. It is estimated that between 5 and 10% of pancreatic cancers may have a familial component.
- **Cigarette smoking:** 25% of patients with pancreatic cancer are or have been long-term cigarette smokers. This habit has a greater effect if the patient has one of the aforementioned genetic syndromes.
- **Age:** The risk of pancreatic cancer increases with age. Pancreatic cancer is mostly diagnosed between 60 and 80 years of age.
- **Obesity:** There is evidence that suggests that the risk of pancreatic cancer may increase slightly with increasing body mass index. Body mass index is a measurement that compares weight and height, and it is used as an indicator of obesity or being underweight.
- **Chronic pancreatitis:** Chronic pancreatitis, over the course of some decades, increases the risk of pancreatic adenocarcinoma*. This risk is increased by smoking and genetic factors.
- There is an association between pancreatic cancer and diabetes; however it is more likely that diabetes is, in some cases, an early manifestation of pancreatic cancer and not a predisposing factor.
- Alcoholism and high consumption of red and processed meat are suspected to be associated with an increased risk of pancreatic cancer, but the evidence is inconsistent.

HOW IS PANCREATIC CANCER DIAGNOSED?

There are no current screening¹ programs that can be recommended to the general public due to the fact that there are no ideal screening methods for pancreatic cancer. Early stage and premalignant lesions*of pancreatic cancer do not cause symptoms. Therefore, early detection of pancreatic cancer is difficult and infrequent. However, for patients that have any of the hereditary conditions mentioned above regular endoscopic ultrasound (EUS) that allows detection of small lesions and magnetic resonance imaging (MRI) is advised.

Pancreatic cancer can be suspected through a number of different symptoms. The main symptoms are weight loss, jaundice, and abdominal pain or back pain. These symptoms can be caused by many other diseases, which can make the diagnosis of pancreatic cancer difficult. Sometimes patients also present with newly diagnosed diabetes or pancreatitis.

The diagnosis of pancreatic cancer is based on the following examinations:

- 1. Clinical examination.** Some of the symptoms that can be detected during clinical examination of a patient with pancreatic cancer are as follows:
 - *Jaundice* is an important feature, but pancreatic cancer is not the only cause of it. Jaundice is the yellowing of the skin and eyes due to an increased level of bilirubin* in the blood. Jaundice can be a consequence of the blockage of the common bile duct by the tumor that in this case is very likely to be located in the head of the pancreas. This will also cause accumulation of bile in the gallbladder which can cause *gallbladder enlargement*. Since the common bile duct is blocked, the bilirubin does not arrive to the intestine and the faeces are whitened. If the bilirubin level in the blood is high, it is excreted from the body through the urine in higher amounts than normal and the urine is darker than usual.
 - *Abdominal and back pain* due to the pressure on nearby structures, including nerves. This mainly occurs if the tumor is located in the body or tail of the pancreas.
 - *Unexpected weight loss* and *poor appetite* are common.
 - *Digestive problems* can occur if the cancer blocks the duct of the pancreas that joins the common bile duct, resulting in a lack of enzymes* to digest fatty meals. This can cause nausea, vomiting and diarrhea.
 - *Blood clots* can appear, although most blood clots have another cause. If the blood clot appears in a deep vein (legs, pelvis or arms) it is known as deep-vein thrombosis*. Rarely, a piece of the blood clot can be released in the blood flow and end up in an artery of the lungs (pulmonary embolism) causing chest pain and shortness of breath.
 - *Uneven texture of the fatty tissue* underneath the skin (lipodystrophy) can develop and is caused by the release of the pancreatic enzymes* that digest fat.

¹ Screening consists of performing an examination in order to detect cancer at an early stage, before any sign of the cancer appears. A systematic screening is proposed if a safe and acceptable examination can be performed and if this examination is able to detect cancer in the majority of cases. It should also be proven that treating screened cancers is more effective than treating cancers diagnosed because signs of cancer were present.



- *Problems with sugar metabolism* and rarely *diabetes*, which can be recognised through a laboratory test and are due to the destruction of the cells that produce insulin* in the pancreas.
- *Pancreatitis* is an inflammation of the pancreas and can be caused by pancreatic cancer, especially in the elderly when no other obvious reason is causing the pancreatitis like gallstones or alcohol abuse. But symptoms of pancreatitis (mainly pain, nausea and vomiting) are also not unique to pancreatic disease, which can make its diagnosis difficult.

2. Radiological examination*. When pancreatic cancer is suspected abdominal ultrasound is usually the initial examination. For further evaluation endoscopic ultrasound (EUS), contrast-enhanced multi-detector computed tomography (MD-CT), and magnetic resonance imaging (MRI), this together with magnetic resonance cholangiopancreatography (MRCP) have the highest sensitivity for not only detection of pancreatic cancer but to provide additional information on the pancreatic and the bile ducts.



EUS is an endoscopy combined with ultrasound to obtain images of internal organs which allows biopsy and/or fine needle aspiration cytology. *MRCP* helps to visualize the pancreatic and bile ducts in a non-invasive manner. *MD-CT* and *MRI* allow evaluation of invasion of vessels and metastasis (e.g. lymph nodes, liver, peritoneal cavity).

Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure in which an endoscope is used to reach the upper part of the digestive system until the first part of the small intestine. It has a role only to relieve bile duct obstruction by the pancreatic tumor. However, in the preoperative setting, ERCP and placement of a stent in the bile ducts should only be performed if surgery cannot be done expeditiously.

3. Laboratory tests. CA 19.9* is a carbohydrate that can be produced by cancer cells of the pancreas and found in the blood where it can be measured from a blood sample. Some patients with pancreatic cancer may have an elevated level of CA 19.9, (tumor marker*) whereas others may not. But CA19.9 can also be elevated for other reasons than pancreatic cancer, so it is not specific for pancreatic cancer. The level of CA 19.9 in the blood is not very useful for making a diagnosis but it is often useful to get a baseline level in order to evaluate the response to treatment and for follow-up.



4. Histopathological* examination. This is the laboratory examination of the tumor cells by taking a sample of the tumor (a biopsy*). This laboratory examination is performed by a pathologist* who will confirm the diagnosis of pancreatic cancer and will give more information on the characteristics of the cancer. It is mandatory in the case of tumors that cannot be removed





by surgery or if another treatment is planned before surgery.

There are 2 ways to obtain a sample of the tumor, but when the tumor cannot be removed by surgery (unresectable) only the first one is recommended:

- Fine needle aspiration biopsy is a procedure in which the doctor inserts a thin needle either through the skin using CT scan as guide, or directly into the pancreas via an endoscope using EUS. The latter is preferred because the risk of seeding* tumor cells is lower with this method. Using CT scan* or EUS images to view the position of the needle helps the doctor to be sure of reaching the tumor correctly, and then small tissue samples are removed. The main advantages of fine needle aspiration biopsy are that the patient does not require general anesthesia* and major side effects are rare.
- Doctors use laparoscopy* (sometimes called keyhole surgery) as a way of looking at and removing a piece of the pancreas (biopsy). Patients are usually sedated for this procedure. The surgeon makes several small incisions to the abdomen and inserts small telescope-like instruments into the abdominal cavity. One of these is usually connected to a video monitor. The surgeon can view the abdomen and see how big the tumor is and whether it has spread and may take tissue samples as well. This method is not recommended in the case of a tumor that cannot be removed by surgery.

Biopsy* is mandatory if the tumor cannot be removed by surgery or when another treatment is planned before surgery. In the presence of metastases*, biopsy of a metastasis can be taken under ultrasound* and CT-scan* guidance.

For patients expected to undergo radical surgery a previous biopsy is not necessary. Furthermore, preoperative percutaneous (a needle is inserted through the skin to reach the tumor) sampling should be avoided. Nevertheless, after surgery an examination of the tumor cells will be planned to confirm the diagnosis.



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 best treatment.



Relevant information about the patient

- Resectability of the tumor (whether the tumour can be removed through surgery or not)
- Personal medical history
- History of cancer in relatives, especially pancreatic cancer
- History of cigarette smoking
- Results from the clinical examination by the doctor
- General well-being
- Before the operation, a pre-operative evaluation will be performed to assess the risks of the anaesthesia* and the risks of the operation. A pre-operative evaluation consists of specific questions and a physical examination. It usually requires a chest X-ray* and blood tests to assess the white blood cell*, red blood cell* and platelet* count, as well as haemoglobin* level, liver function and kidney function. Some additional examinations may be necessary according to the medical history of the patient.

Relevant information about the cancer

- **Staging**

Doctors use staging to assess the extent of the cancer and the prognosis* of the patient. The TNM staging system is commonly used. The combination of size of the tumor and invasion of nearby tissue (T), involvement of lymph nodes* (N), and metastasis* or spread of the cancer to other organs of the body (M), will classify the cancer into one of the stages described in the table below.

The stage is fundamental for decisions regarding treatment. The less advanced the stage, the better the prognosis. Staging is usually performed twice: after clinical and radiological examination* and after surgery. Contrast-enhanced multi-detector computed tomography (MD-CT) or magnetic resonance imaging (MRI), together with magnetic resonance cholangiopancreatography (MRCP) should be used for staging and they can be complemented by endoscopic ultrasound (EUS) because the latter provides information on vessel invasion and potential involvement of lymph nodes. EUS is also the preferred means to obtain a biopsy of the pancreas. MD-CT of the chest is recommended to evaluate potential lung metastases. If surgery is performed, staging may also be influenced by the laboratory examination of the tumor removed.

The table below presents the different stages for pancreatic cancer. The definitions are very technical so it is recommended to ask doctors for more detailed explanations.



Stage	Definition
Stage 0	The cancerous cells are located within the top layers of cells of the pancreas and have not invaded deeper tissues. The cancer has not spread outside the pancreas. These tumors are sometimes referred to as pancreatic carcinoma* in situ or pancreatic intraepithelial neoplasia III (PanIn III).
Stage IA	The tumor <ul style="list-style-type: none"> - has not spread outside the pancreas, neither to lymph nodes* nor to other parts of the body; - and is less than 2 cm in diameter.
Stage IB	The tumor <ul style="list-style-type: none"> - is still confined to the pancreas but is more than 2 cm in diameter; - and has not spread to lymph nodes* or other parts of the body.
Stage IIA	The tumor <ul style="list-style-type: none"> - has grown outside the pancreas, into the duodenum, bile duct or other tissues that surround the pancreas except large blood vessels and major nerves; - and has not spread to lymph nodes* or other parts of the body.
Stage IIB	The tumor <ul style="list-style-type: none"> - has spread to lymph nodes* but not to other parts of the body; - and may or may not be growing outside the pancreas, into the duodenum, bile duct and other tissues that surround the pancreas without invading large blood vessels and major nerves.
Stage III	The tumor <ul style="list-style-type: none"> - has grown outside the pancreas into nearby large blood vessels or major nerves; - and may or may not have spread to nearby lymph nodes*. It has not spread to other parts of the body.
Stage IV	The cancer has spread to other parts of the body (metastasis*).

- **Results of the biopsy***

Biopsy is mandatory if the patient will not receive surgical treatment, because the tumor cannot be removed, or when chemotherapy* is indicated for a period before surgery (neo-adjuvant therapy). In the presence of metastasis*, biopsy should be taken from them under ultrasound* or CT* guidance.

- **Histological* type**

The histological type indicates the type of cells that makes up most of the tumor. Cancer cells usually present characteristics of the tissue they arise from. Pancreatic adenocarcinomas are the most frequent type of pancreatic cancer. They arise from the ducts of the pancreas. Although they can appear anywhere in the pancreas, they are most commonly found in the head of the pancreas, so their symptoms are associated with the blockage of nearby structures like the bile duct, i.e. jaundice. They are also associated with diabetes.

- **Surgical margins**

When a tumor is removed surgically the histopathology report will also provide information on the presence of cancer cells on the surface of the tissues that have been removed (margins). Many cases are considered to be still microscopically invading surrounding tissues, because cancer cells are found on the external part of the tissues that have been removed. This happens to be the case in up to 75% of patients that undergo surgery with curative intent. It is considered that if cancer cells are found at less



than 1 mm from the surface of the resected tissues, surrounding tissues must be regarded as invaded by cancer.

- **Positive lymph nodes**

During surgery lymph nodes are also removed and they are sent to histopathology to analyze how many of them are invaded by cancer (in general such nodes are called positive lymph nodes).

- **Grade**

Grade is based on how different from normal pancreatic cells the tumor cells look and on how quickly they grow. For pancreatic cancer the tumor grade will be between 1 and 4.

Grade 1: Similar to normal pancreatic cells

Grade 2: Moderately similar to pancreatic cells

Grade 3: Barely similar to pancreatic cells

Grade 4: Different from pancreatic cells

The lower the grade, the better the prognosis*.

- **Tumor resectability**

A pancreatic tumor is frequently considered unresectable when it appears to be invading adjacent tissues, other organs in the body, lymph nodes* and nearby blood vessels.

Laparoscopy or keyhole surgery, sometimes used for biopsy sample as already explained may detect small peritoneal and liver invasion (metastasis). This can change the therapeutic approach in up to 15% of patients. It can be performed before removal of left-sided large pancreatic tumors and/or in case of high CA19.9 levels or when neoadjuvant treatment is considered. However, the extent of the cancer can often be accurately determined only during surgery.

WHAT ARE THE TREATMENT OPTIONS?

Planning of the treatment involves an interdisciplinary 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 possibility of curing the cancer depends on whether the tumor is surgically removable (resectable) or not. A tumor is considered resectable when it appears to be localized in the pancreas, not invading adjacent tissues or other organs in the body.

The treatments listed below have their benefits, their risks and their contraindications. It is recommended that patients ask oncologists* about the expected benefits and risks of every treatment in order to be informed of the consequences of the treatment. For some treatments, several options are available and the choice should be discussed after weighing up their respective risks and benefits.

Treatment plan for stage 0, IA and IB

At these stages the tumor is confined to the pancreas and has not spread to lymph nodes or other parts of the body.*

For these stages, the standard treatment option is removal of the whole or part of pancreas together with other tissues or organs located next to the pancreas. Different surgical techniques exist according to where the tumor is located. Additional chemotherapy* is suggested.

Surgery

When the cancer affects the head of the pancreas, a pylorus-preserving pancreaticoduodenectomy is the procedure of choice:



- The head of the pancreas is removed;
- The bile duct, the gallbladder, the duodenum (first part of the small intestine) and part of the stomach (preserving the last part of the stomach and the pylorus) are removed as well due to the fact that they receive blood from the same artery as the head of the pancreas. If the pancreas were removed alone, the blood flow to these organs would be affected and they would become necrotic*.
- The remaining pancreas, bile duct and stomach are re-joined to the intestine.



When the cancer affects the body and tail of the pancreas, a distal pancreatectomy with splenectomy is performed:

- The body and tail of the pancreas are removed (distal pancreatectomy);
- The spleen is removed as well (splenectomy), due to the fact that the spleen and the body and tail of the pancreas receive blood from the same artery. If only the body and tail of the pancreas were removed, the blood flow to the spleen would be affected and it would become necrotic*.

Adjuvant therapy

An adjuvant therapy is a therapy given in addition to surgery. Clinical trials clearly show that the best current adjuvant treatment is chemotherapy.

After surgery, chemotherapy either with gemcitabine* or 5-fluorouracil* is recommended. This approach improves life expectancy in some patients with tumors resected completely and in patients whose tumors have invaded surrounding tissues, which can be observed microscopically but not to the naked eye. Gemcitabine and 5-fluorouracil* (5-FU) are similarly effective. However, gemcitabine treatment is associated with less toxic side effects compared to 5-FU. The respective risks and benefits of each drug should be discussed with doctors.

Today, there is no proof of advantage of chemoradiation over chemotherapy alone, so it should be performed only within clinical trials or may be suggested outside a clinical trial if the analysis of the tumor in the laboratory shows that the whole tumor has not been removed. There is no evidence for a particular benefit of chemoradiation when the tumor is larger than 3 cm.

Chemoradiation is the use of chemotherapy* and radiotherapy* to treat the cancer. Radiotherapy is the use of radiation to kill cancer cells. Cancer cells are less capable of recovery from radiation than normal cells. The radiation is aimed at the tumor of the patient from a device outside the body and is a local treatment modality.

Treatment plan for stage IIA

The tumor has grown outside the pancreas, into the duodenum, bile duct and other tissues that surround the pancreas except large blood vessels and major nerves. It has not spread to lymph nodes or other parts of the body.*

The standard treatment when the tumor is resectable is removal of the pancreas, otherwise there are some therapies used to relieve the symptoms produced by the cancer.

When the tumor is resectable

Surgery

Pancreatic removal is the standard treatment.

Even after doing imaging tests and laparoscopy*, surgery may be stopped during the operation if the surgeons find that the tumor has spread beyond the pancreas and it is not possible to remove it completely. In these cases a sample of the tumor should be taken to confirm the diagnosis.



Intraoperative radiotherapy, which is the delivery of radiotherapy during surgery is still an experimental approach and it is not recommended as a routine treatment. It involves the irradiation of the area where the tumor was, before closing the surgical incision. It helps to control the tumor growth, but it is not known if this approach is able to prolong the life of the patients compared to the radiotherapy after surgery. The possible benefit of intraoperative radiotherapy over radiotherapy after surgery is being investigated.

Neoadjuvant therapy

When the pancreatic cancer is resectable, chemotherapy or the combination of chemotherapy and radiotherapy (called chemoradiation) before surgery should only be performed within the setting of clinical trials because so far not sufficient evidence that this strategy is better than immediate surgery is available. Administering chemotherapy or chemoradiation before surgery is called neoadjuvant therapy by doctors.

Even if the evidence is limited, the current understanding of the biology of pancreatic cancer suggests that this strategy might be useful. Several trials examining this strategy are presently under way.

When the tumor is unresectable (This could be the case for many patients at this stage of the disease and is called locally advanced pancreatic cancer):

Multimodal treatment

In case of larger tumors that could be resectable or in case of unresectable tumors, some patients may benefit from chemotherapy or chemoradiation to achieve downsizing of the tumor so that it turns out into a resectable stage.

Patients who develop metastases during neoadjuvant treatment, or whose primary tumor progresses locally are not candidates for surgery and should continue with treatment options considered for patients with advanced stage of the disease. .

The optimal strategy in this setting is still under clinical investigation and so far, there is no standard protocol for neoadjuvant chemoradiotherapy in Europe.

Surgery

If the tumor is causing intestinal obstruction, the patient can benefit from a palliative bypass* to relieve it. This is achieved surgically by creating a connection between the stomach and the part of the intestine located after the obstruction. This procedure, as any surgical procedure, may lead to complications. Surgery should be followed by chemotherapy*, or chemoradiotherapy.

Adjuvant therapy

After surgery, chemotherapy* with either gemcitabine* or 5-fluorouracil*(5-FU) is recommended. This approach improves life expectancy of some patients whose tumor was resected completely. This approach can also improve life expectancy of patients whose tumor was initially thought not to have invaded surrounding tissues when examined with the naked eye during the operation but turned out to have actually invaded surrounding tissues after the resected tumor was examined in the lab under the microscope. Gemcitabine and 5-fluorouracil* are similarly effective. However, gemcitabine



treatment is associated with less toxic side effects compared to 5-FU. The respective risks and benefits of each drug should be discussed with doctors.

Today, there is no proof of advantage of chemoradiation over chemotherapy alone, so it should be performed only within clinical trials or may be also suggested if the analysis of the tumor in the laboratory shows that the whole tumor has not been removed. There is no evidence for a particular benefit of chemoradiation when the tumor is larger than 3 cm.

Chemoradiation is the use of chemotherapy* and radiotherapy* to treat the cancer. Radiotherapy is the use of radiation to kill cancer cells. Cancer cells are less capable of recovery from radiation than normal cells. The radiation is aimed at the tumor of the patient from a device outside the body and is a local treatment modality.

The toxicity of these therapies is common and they can cause nausea and/or vomiting, diarrhea, neutropenia* and anemia*.

Treatment plan for stage IIB and III

The tumor has grown outside the pancreas, into the duodenum, bile duct and other tissues that surround the pancreas except large blood vessels and major nerves and has spread to the lymph nodes but not to other parts of the body. It may also have invaded large blood vessels and major nerves, independent of the invasion of the lymph nodes.*

The majority of patients with stage IIB and III have large tumors or tumors that encase blood vessels, which prevent the complete removal of the tumor by surgery. These patients may benefit from preoperative (neoadjuvant) chemotherapy or chemoradiation to achieve downsizing of the tumor so that it could be resectable afterwards.

The optimal neoadjuvant strategy is still under investigation and there is so far no standard protocol for neoadjuvant chemotherapy in Europe.

The options for preoperative therapy for these patients could be:

- **Chemotherapy**
- **Chemoradiation**
- **Chemotherapy* followed by chemoradiation**

For the majority of patients with stage IIB and III disease, the tumor is unresectable. The treatment relies generally on chemotherapy. Alternatively, chemotherapy followed by a combination of chemotherapy and radiotherapy may be considered for patients with locally advanced disease.

Chemoradiation: Radiotherapy combined with 5-fluorouracil* can be considered. The results of a better outcome compared to chemotherapy alone are not conclusive yet.

Chemotherapy followed by chemoradiation: Patients could be treated with gemcitabine* and if after three months their tumors do not progress and they maintain good performance status, 5-fluorouracil* based chemoradiation can be added with intention to improve life expectancy.

Treatment plan for stage IV

The cancer has spread to other parts of the body.

Curative attempt is not an option at this point but efforts to ease symptoms should be made.

Chemotherapy*

The use of chemotherapy at this stage can help to shrink the cancer, improve symptoms, patient's well-being and ability to function, and help patients to live longer.

Patients should be followed at each cycle of chemotherapy for side effects and evaluated for response to chemotherapy every eight weeks. Clinical examination and ultrasound may be useful tools to assess the course of disease in this stage of the disease. When performing abdominal ultrasound patients should be monitored for the presence of ascites* that can indicate a spread of the tumor within peritoneal cavity.

Gemcitabine* alone is still the standard chemotherapy for patients with metastatic pancreatic cancer.

Many combinations of gemcitabine with other drugs have been tried so far, none has shown evident advantages with respect to prolonging life expectancy of the patients. However, recently the combination of gemcitabine plus nab-paclitaxel is superior to gemcitabine treatment alone. Therefore this combination can be recommended for patients with metastatic pancreatic cancer. However, the toxicity of this protocol is higher compared to gemcitabine alone.

Recently a study that investigated a combination of 3 chemotherapeutic agents, 5-fluorouracil*, oxaliplatin* and irinotecan* (the so called FOLFIRINOX regimen) showed interesting results in terms of extending life and delaying deterioration of quality of life. However, it is important to note that the patients who participated in the study were younger than 75 years and were in good general condition. Patients treated with FOLFIRINOX experience more side effects than those treated with gemcitabine alone. Due to the improvements in the treatment outcomes, FOLFIRINOX can be considered as a novel therapeutic option for patients of 75 years old or younger, in good general condition and with an appropriate liver function.

Chemotherapy combinations with targeted therapies have at large been disappointing. Only a combination of gemcitabine with erlotinib* has been approved for use in Europe, but it has a modest overall gain in life expectancy. The combination treatment appears to be efficient in patients who develop skin rash within 8 weeks of treatment with erlotinib. The high economic cost of such combination and modest improvements in terms of efficacy in the majority of the patients question its role for general use in patients with metastatic pancreatic cancer.

After progression of cancer under first-line treatment, there is no established standard chemotherapy protocol. However, 5-fluorouracil*/oxaliplatin* is a combination of chemotherapy drugs that has been shown beneficial after progression on gemcitabine in clinical trials, so it can be considered in this setting. In patients whose disease progressed while being treated with FOLFIRINOX as first-line treatment, gemcitabine can be considered as second-line treatment. In all cases, patients should consider the possibility of undergoing treatment in the context of a clinical trial* if available.

Palliative and supportive therapy*

Treatment of some symptoms can improve quality of life in patients with pancreatic cancer, these are:

Jaundice

Jaundice as a consequence of biliary obstruction is common in patients with cancer that affects the head of the pancreas. To relieve it an artificial tube (stent) should be inserted endoscopically* or via needle-puncture of the skin into the biliary ductal system. It is preferred to insert the stent endoscopically, as this route is associated with a lower frequency of complications. In patients who have a life expectancy of more than three months, metal stents should be preferred over the plastic ones because they cause fewer complications (such as e.g. occlusion). Plastic stents should be replaced at least every 6 months to avoid stent occlusion. When the placement of a stent is not possible a percutaneous drainage of the bile is recommended. The fact that jaundice is caused by a biliary duct obstruction has to be established in advance, e.g. by abdominal ultrasound.

Gastrointestinal obstruction

If a patient presents with duodenal or gastric outlet obstruction, the insertion of a stent can relieve this complication.

Less than 5% of patients with pancreatic cancer present with duodenal obstruction, which can be relieved by a metal stent. Gastric outlet obstruction may be more common during the course of the disease and drugs that enhance gastrointestinal motility such as metoclopramide can be useful to speed gastric emptying.

For some patients, the obstruction can be bypassed by joining the stomach to the part of the intestine after the obstruction (gastroenterostomy), although it is not considered a standard treatment.

Pain

Patients who have severe pain must take opioids*. Morphine* or morphine derivatives are generally the drug of choice. People often prefer to take it orally but it can also be administered in a vein or as a sticky patch put on the skin if the patient has impaired swallowing or gastrointestinal obstruction.

Radiotherapy given less often than once a day may be delivered to improve the pain control and reduce analgesic* consumption.

Celiac plexus* (a network of nerves located in the back part of the stomach) blockade using an analgesic and administered via a needle placed through the skin can be considered, especially for patients who tolerate opioids* poorly. Analgesic response rates as high as 50-90% are reported with between 1 month and 1 year duration of effect. This procedure consists of injection (either through the skin under the guidance of a CT-scan or through the gastric wall with an endoscopic* ultrasound*) of bupivacaine* and alcohol around the celiac plexus.



RELIABLE CANCER THERAPIES



European Society for Medical Oncology

Nutrition

If possible, the nourishment of the patient via mouth is the preferred route. Nevertheless, short-term parenteral nutrition (i.e. endovenous nutrition) is commonly accepted in patients with acute gastrointestinal complications from chemotherapy and radiotherapy and even its use might be extended to be continued at home in patients with gastrointestinal complications from radiotherapy. Parenteral nutrition at home is also recommended in patients who are unlikely to recover, and who have trouble being fed by mouth due to obstruction in the digestive tract. It can help patients with advanced disease and progressive cachexia* to stabilize their nutritional status.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE THERAPIES?

Side effects of the aforementioned therapies are common.

Complications of surgery

Bleeding is a very common complication after surgery. Other side effects can include a delay in emptying of the stomach and consequently nutritional deficiency and leakage of pancreatic juices that can digest and destroy surrounding tissues.

The pancreas produces important enzymes* and hormones for digestion. When the pancreas is removed, those enzymes are no longer or insufficiently produced, resulting in malabsorption syndrome, the failure to completely absorb nutrients from the gastrointestinal tract. Taking supplements of pancreatic enzymes orally can aid digestion. Nevertheless long-term gastrointestinal dysfunction occurs in very few patients after surgery.

If the pancreas is removed completely (total pancreatectomy), diabetes will occur as a consequence of the absence of production of insulin which is only made by the pancreas. Personalized insulin treatment should be initiated with specialists when this occurs.

Side effects of chemotherapy

Side effects of chemotherapy* are very frequent. They will depend on the drug(s) administered, on the doses and on individual factors. Combinations of different drugs usually lead to more side effects than the use of a single drug.

- Gemcitabine* can produce flu-like symptoms, fever, tiredness, nausea and vomiting, poor appetite, skin rash and decrease of the number of platelets, red and white blood cells.
- Side effects of each drug in the FOLFIRINOX combination (5-fluorouracil, irinotecan and oxaliplatin) are listed below separately. However, the most frequent side effects of this drug combination are low levels of white blood cell (neutropenia), fever and infections due to low levels of white blood cell, and low levels of platelets.
 - 5-fluorouracil* can cause diarrhea, nausea and vomiting, mouth sores, poor appetite, photophobia (sensitivity of the eyes to light), taste changes and decrease of the number of platelets*, red and white blood cells*.
 - Oxaliplatin* can damage peripheral nerves, cause nausea and vomiting and reduce the amount of platelets and red and white blood cells. Hearing can sometimes be affected, as well as the kidneys and liver. It can also cause diarrhea.
 - Irinotecan can cause diarrhea, hair loss, weakness and low blood cells counts.
- Capecitabine* can reduce the amount of red blood cells* (anemia*), cause tiredness, diarrhea, nausea and vomiting. Redness, swelling, peeling of the skin of the palms and soles (hand-foot syndrome) is another common side effect caused by capecitabine.
- Erlotinib* can cause skin rash, diarrhoea, poor appetite, tiredness, shortness of breath, coughing, nausea and vomiting.

Side effects of radiotherapy

Radiotherapy directed to the area of the pancreas can cause nausea, vomiting, diarrhea and tiredness.

WHAT HAPPENS AFTER THE TREATMENT?

Follow-up after surgery with doctors

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



- Detect possible recurrence*
- Evaluate treatment-related complications and treat them
- Provide psychological support and information to enhance returning to normal life

Follow-up visits with the oncologist* should include:

- **History-taking:** (reviewing the patient's medical history) especially when abdominal and/or back pain occurs, along with a complete physical examination.
- **Radiological examination*:** taking an abdominal CT scan* every 6 months for a period of 2 years. CT scans in locally advanced disease may be indicated in order to rule out the presence of metastasis* and therefore to add radiotherapy to the treatment.
- **Blood tests:** monitoring amylase* and CA 19.9* levels, among other routine exams, could be performed every 3 months for a period of 2 years. It should be especially a case if it was elevated before the surgery.

However, early detection of a possible recurrence has no clear advantage in terms of outcome.

Returning to normal life

It can be hard to live with the idea that the cancer can come back. From what is known today, no specific way to decrease the risk of recurrence* after completion of treatment can be recommended. As a consequence of the cancer itself and of treatment, return to normal life may not be easy for some people. Questions related to body image, fatigue, work, emotions or lifestyle may be a concern for the patient. Discussing these questions with relatives, friends or doctors may be helpful. Support from ex-patients' groups or telephone information and helplines as well as counseling by specialized psycho-oncologists are available in many countries

What if the cancer comes back?

If the cancer comes back it is called recurrence* and the treatment depends on the extent of the recurrence. If the cancer comes back, it is usually within the first two years following the surgery. The extent of the recurrence should be fully evaluated by physical examination, radiological examination* and blood tests. Discussion of treatment options should be done in a multidisciplinary meeting.

Unfortunately, recurrence of pancreatic cancer is very frequent after surgical treatment. There are factors that are associated with the risk of recurrence, for example having high levels of the serum



RELIABLE CANCER THERAPIES



European Society for Medical Oncology

marker* CA 19.9* after surgery. The average time between surgery and radiological detection of tumor recurrence has been shown to be longer in patients with normal post-operative CA 19.9.

Chances for cure are limited, even for recurrences diagnosed early, so a follow-up schedule should be discussed with the patient and designed to avoid emotional stress and economic burden for the patient.

DEFINITIONS OF MEDICAL TERMS

5-fluorouracil

A drug used to treat symptoms of cancer of the colon, breast, stomach, and pancreas. It is also used in a cream 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.

Adenocarcinoma

Cancer that begins in cells that line certain internal organs and that have gland-like (secretory) properties.

Amylase

An enzyme* that helps the body digest starches.

Anaemia

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.

Analgesic

A drug that reduces pain. Analgesics include aspirin, acetaminophen, and ibuprofen.

Anaesthesia

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

Bilirubin

Substance formed when red blood cells* are broken down. Bilirubin is part of the bile, which is made in the liver and is stored in the gallbladder. The abnormal buildup of bilirubin causes jaundice*.

Biopsy

The removal of cells or tissues 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.

Bupivacaine

A drug used to relieve pain by blocking signals at nerve endings. It is being studied in the relief of pain following surgery for cancer. It is a type of local anesthetic*.

CA 19.9

A substance released into the bloodstream by both cancer cells and normal cells. Too much CA 19-9 in the blood can be a sign of pancreatic cancer or other types of cancer or conditions. The amount of



CA 19-9 in the blood can be used to help keep track of how well cancer treatments are working or if cancer has come back. It is a type of tumor marker*.

Cachexia

A condition in which the patient loses weight and muscle tissue and is weak and tired. A loss of appetite is also associated.

Capecitabine

Capecitabine is a cytotoxic medicine that belongs to the group antimetabolites. Capecitabine is a 'prodrug' that is converted to 5-fluorouracil (5-FU) in the body, but more is converted in tumor cells than in normal tissues. It is taken as tablets, while 5-FU, an analogue of pyrimidine, normally needs to be injected. Pyrimidine is part of the genetic material of cells (DNA and RNA). In the body, 5-FU takes the place of pyrimidine and interferes with the enzymes* involved in making new DNA. As a result, it inhibits the growth of tumor cells and eventually kills them.

Carboplatin

A drug that is used to treat advanced ovarian cancer that has never been treated or symptoms of ovarian cancer that has come back after treatment with other anticancer drugs. It is also used with other drugs to treat advanced, metastatic*, or recurrent* non-small cell lung cancer and is being studied in the treatment of other types of cancer. Carboplatin is a form of the anticancer drug cisplatin and causes fewer side effects in patients. It attaches to DNA in cells and may kill cancer cells. It is a type of platinum compound.

Carcinoma

Cancer that begins in the skin or in tissues that line or cover internal organs.

Catheter

A tube that can be inserted into the body. It has many uses, including draining or administering fluids or gases.

Celiac plexus

A network of nerves in the abdomen, behind the stomach. It, amongst other functions, conducts pain sensation from the abdominal organs, including the liver, spleen, stomach, and pancreas to the brain.

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.

Clinical trial

A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called clinical study.

Computed tomography (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.

Cytological

Of or relating to cytology, which is the science that studies the structure and function of the cells.

Endocrine

The endocrine system is a system of glands. Glands secrete hormones in the blood. These hormones have different functions, such as mood control or growth.

Endoscopy

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.

Enzyme

A protein that speeds up chemical reactions in the body.

Erlotinib

Erlotinib is an anticancer medicine that belongs to the group 'EGFR inhibitors'. Erlotinib blocks EGFRs, which can be found on the surface of some tumor cells. As a result of this block, the tumor cells can no longer receive the messages needed for growth, progression and spreading (metastasis*). As a result, erlotinib helps to stop the cancer from growing, multiplying and spreading through the body.

Exocrine

Of or relating to exocrine glands or their secretions. Exocrine glands are organs that discharge their secretions externally, either directly or through a duct, contrary to them other glands (endocrine glands) discharge their secretions to the bloodstream.

Familial Atypical Multiple Mole Melanoma Syndrome

An inherited condition marked by the following: (1) one or more first- or second-degree relatives (parent, sibling, child, grandparent, grandchild, aunt, or uncle) with malignant melanoma; (2) many moles, some of which are atypical (asymmetrical, raised, and/or different shades of tan, brown, black, or red) and often of different sizes; and (3) moles that have specific features when examined under a microscope. FAMMM syndrome increases the risk of melanoma and may increase the risk of pancreatic cancer. Also called FAMMM syndrome.

Gemcitabine

The active ingredient in a drug that is used to treat pancreatic cancer that is advanced or has spread. It is also used with other drugs to treat breast cancer that has spread, advanced ovarian cancer, and non-small cell lung cancer that is advanced or has spread. It is also being studied in the treatment of other types of cancer. Gemcitabine blocks the cell from making DNA and may kill cancer cells. It is a type of antimetabolite.

Glucagon

A hormone produced by the pancreas that increases the level of glucose* (sugar) in the blood.

Glucose

Glucose is a monosaccharide sugar that occurs widely in plant and animal tissue. It is the major energy source of the body.

Haemoglobin

The substance inside red blood cells* that binds to oxygen in the lungs and carries it to the tissues.

Histological

Of or relating to histology, which is the study of animal and plant tissues using a microscope.

Histopathological

The study of diseased cells and tissues using a microscope.

Insulin

A hormone made in the pancreas. Insulin controls the amount of sugar in the blood by moving it into the cells, where it can be used by the body for energy.

Irinotecan

The active ingredient in a drug used alone or with other drugs to treat colon cancer or rectal cancer that has spread to other parts of the body or has come back after treatment with fluorouracil. It is also being studied in the treatment of other types of cancer. Irinotecan blocks certain enzymes* needed for cell division and DNA repair, and it may kill cancer cells. It is a type of topoisomerase inhibitor and a type of camptothecin analog.

Jaundice

A condition in which the skin and the whites of the eyes become yellow, urine darkens, and the color of stool becomes lighter than normal. Jaundice occurs when the liver is not working properly or when a bile duct is blocked.

Laparoscopy

An operation where surgical instruments are introduced in the abdomen or in the pelvis through small incisions and with the help of a camera.

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.

Magnetic resonance imaging (MRI)

An imaging technique that is used in medicine. It uses magnetic resonance. Sometimes, a fluid is injected that enhances the contrast between different tissues to make structures more clearly visible.

Marker

A diagnostic indication that a disease may develop.

Metastasis

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.



Morphine

A drug used to treat moderate to severe pain. It binds to opioid receptors in the central nervous system and some other tissues. Morphine sulfate is made from opium. It is a type of opiate and a type of analgesic* agent.

Multidisciplinary opinion

A treatment planning approach in which a number of doctors who are experts in different specialties (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.

Mutation

A change in the sequence of base pairs in the DNA that makes up a gene. Mutations in a gene do not necessarily change the gene permanently.

Necrosis/necrotic

Refers to the death of living tissues.

Neuroendocrine

Having to do with the interactions between the nervous system and the endocrine system. Neuroendocrine describes certain cells that release hormones into the blood in response to stimulation of the nervous system.

Neutropenia

A condition in which there is a lower-than-normal number of neutrophils, a type of white blood cell*. It may be seen with viral infections and after radiation and chemotherapy*. It lowers the immunologic barrier to bacterial and fungal infections.

Non-polyposis colorectal cancer

The hereditary colorectal cancer type where polyps (growths that stick out of the lining of the colon or rectum) do not occur. This in contrast to the inherited Familial Adenomatous Polyposis (FAP) where hundreds to thousands of polyps develop in the colon.

Oncologist

A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation.

Opioids

A substance used to treat moderate to severe pain. Opioids are like opiates, such as morphine* and codeine, but are not made from opium. Opioids bind to opioid receptors in the central nervous system. Opioids used to be called narcotics. An opioid is a type of alkaloid.

Oxaliplatin

A drug used with other drugs to treat colorectal cancer that is advanced or has come back. It is also being studied in the treatment of other types of cancer. Oxaliplatin attaches to DNA in cells and may kill cancer cells. It is a type of platinum compound. Also called Eloxatin.

Palliative bypass

In the context of pancreatic cancer, it is a connection created surgically between the stomach and the intestine, to relieve the intestinal obstruction when the pancreatic tumor is big enough to compress the part of intestine closest to the pancreas, blocking the intestine. So that the food that is being digested avoids the obstructed part of the intestine and passes from the stomach to the part of the intestine free of obstruction.

Palliative therapy

Treatment given to relieve the symptoms and reduce the suffering caused by cancer and other life-threatening diseases. Palliative cancer therapies are given together with other cancer treatments, from the time of diagnosis, through treatment, survivorship, recurrent* or advanced disease, and at the end of life.

Pancreatoblastoma

Rare pancreatic cancer with good prognosis*, the majority of the cases occur during childhood.

Pathologist

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

Peutz-Jeghers Syndrome

A genetic disorder in which polyps form in the intestine and dark spots appear on the mouth and fingers. Having PJS increases the risk of developing gastrointestinal and many other types of cancer. Also called PJS.

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.

Premalignant lesion

Tissue with abnormal appearance in which cancer is more likely to develop in comparison to normal tissue.

Prognosis

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

Radiological examination

Test that uses imaging technology (such as radiography, ultrasound*, computed tomography* and nuclear medicine) to visualize organs, structures and tissues within the body to both diagnose and treat diseases.

Radiotherapy

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



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European Society for Medical Oncology

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 cell

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.

Thrombosis

The formation or presence of a thrombus (blood clot) inside a blood vessel.

Ultrasonography/ultrasound

A procedure in which high-energy sound waves are bounced off internal tissues or organs and make echoes. The echo patterns are shown on the screen of an ultrasound machine, forming a picture of body tissues called a sonogram. Also called ultrasound.

White blood cell

Cells of the immune system* that are involved in the body's defense against infections.

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.