Lung Cancer

you can face it
if you know it better

WALCE
Women Against Lung Cancer in Europe

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you can face it if you know it better

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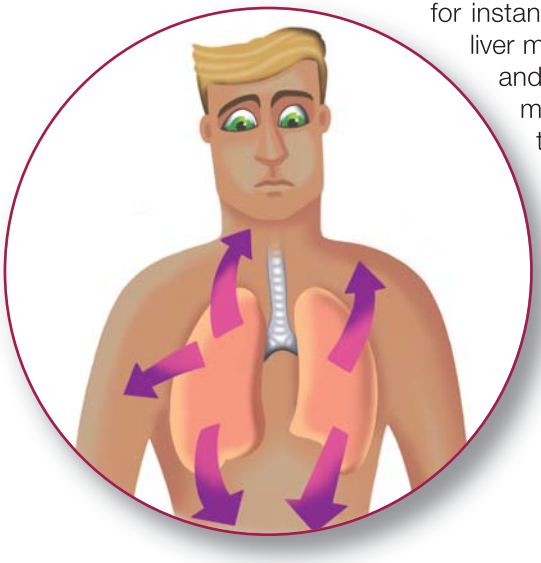
1. Introduction

The term "tumor" refers to a class of diseases characterized by an uncontrolled reproduction of some body cells, that are transformed and begin to multiply in an irregular manner. The cell becomes cancerous when it accumulates a series of damage in the reproduction control system. The proliferation of these abnormal cells leads to the formation of masses within the tissue where they originate, and this is the cancer mass, which may be benign or malignant.

Benign tumors may simply be monitored or can be removed and, in most cases, they do not come back. They never invade other organs or tissues, do not spread to other parts of the body and are rarely a threat to life. Benign lung tumors are very rare, representing no more than 2% of all lung cancers.

Malignant tumors can invade and damage nearby tissues and organs. Cancer cells may (via the bloodstream or lymphatic system) get to other organs or tissues to form there new tumors (**metastases**). The tumor takes its name from the organ where it originates, so for instance it will be termed “lung cancer with liver metastases” or “lung metastatic cancer” and not hepatic cancer (in case of liver metastases) and the therapy will be targeted on cancer lung cells.



2. What causes lung cancer?

A "risk factor" is what increases a person's chance of developing a disease.

The most important risk factor for lung cancer is **cigarette smoking**, which contains many carcinogens that permanently damage cells. The more a person smokes, the higher is the risk of developing cancer, not just lung cancer but also mouth, throat, esophagus, larynx, bladder, kidney, cervix and pancreas.

Thousands of lives could be saved each year if people do not smoke. Effective anti-smoking campaigns should be carried out starting from primary school, but it is important to convince people at any age not to take this dangerous habit or to abandon it. The risk of lung cancer begins to decline slowly as soon as a person quits smoking. The earlier the age at which a person quits smoking, the closer a former smoker's risk of lung cancer will approach the risk for a person who never smoked.

It is never too late to benefit from quitting smoking: even in patients suffering from lung cancer, especially if they have undergone surgery to treat the disease: stop smoking reduces the incidence of relapses (the re-appearance of the disease) and the occurrence of a second tumor.

Although smoking is by far the major cause of lung cancer, is not the only one. Other causes are:

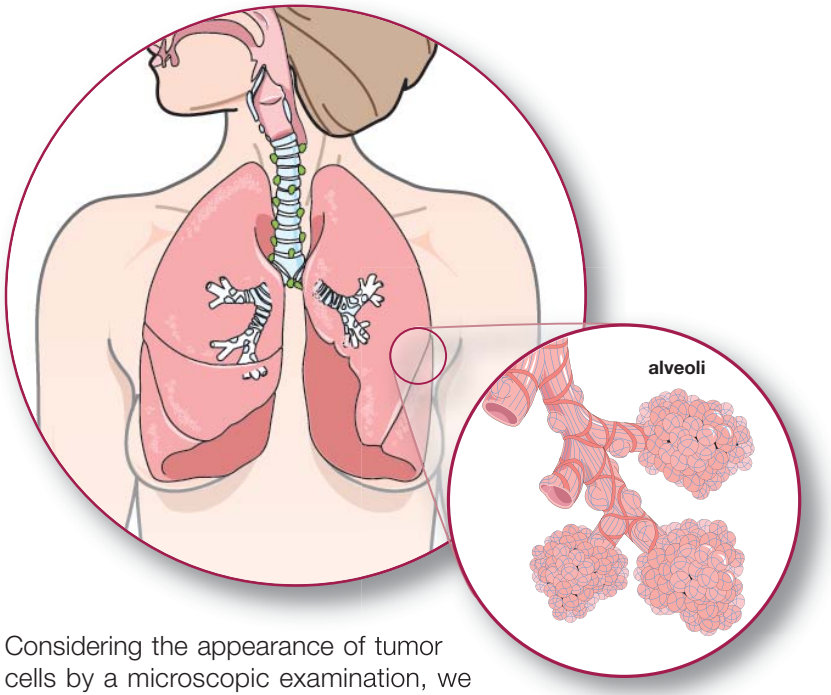
- ***passive smoking:*** exposure to other people's smoke (environmental tobacco smoke) increases the risk of lung cancer among non-smokers.
- ***occupational exposure:*** the workplace exposure to carcinogens - such as asbestos, chromium, arsenic, beryllium and others - increases the risk of developing the disease. Frequently, as in the case of asbestos workers, the risk of developing lung cancer significantly increases if the person smokes and he has an occupational exposure, because the harmful effects of these substances are enhanced by tobacco smoking.

Worker (especially smokers) who are exposed to high levels of radon (a radioactive gas) have an increased risk of developing lung cancer. Radon also can build up in some homes, but generally the levels are much lower than, for instance, in mines.

Apart from "external" causes which increase the risk of getting lung cancer, there is a genetic susceptibility. There are people who may get ill more easily than others and, sometimes (although rarely) even in the absence of external factors. These people unfortunately are not identifiable in advance, since this increased susceptibility to disease depends on several alterations of the genetic code (or DNA), not yet fully identified.

3. Types of lung cancer

Lung cancer arises from cells lining the airways. The airways are the structures carrying the air to the lungs. Lung cancer and bronchial cancer are the same, because the first cell getting sick and becoming a tumor cell is the bronchial one.



Considering the appearance of tumor cells by a microscopic examination, we can distinguish essentially two different categories of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The identification of the tumor type is called "diagnosis" and the diagnosis is essential to guide the doctor in choosing among treatment options. Only in very few cases (usually if there are other diseases or if general conditions of the patient do not allow to get the diagnosis) the type of tumor can not be identified.

Non-small cell lung cancer (NSCLC)

75-80%

Non-small cell lung cancer is more common than small cell lung cancer and accounts for **75-80%** of all cases. The three main kinds of non-small cell lung cancer are named for the type of cells in the tumor, each one with its own variants and subtypes, with similar growth patterns and types of treatment:

30%

- ***squamous cell carcinoma.*** It affects mainly the large bronchi. Accounts for approximately **30%** of all lung tumors and is more common in men or in elderly population of both sexes. It usually does not spread as quickly as other types of lung cancer, remaining localized in the chest taking more time to develop metastases.

40%

- ***adenocarcinoma.*** It develops in the peripheral lung, often involving the **pleura** (ie a serous membrane that covers the lungs and the internal part of the chest wall). Its frequency is around **40%** and it is the most common type among women and non-smokers. In recent years the percentage of adenocarcinoma cases has steadily increased and currently it represents the more frequently type of NSCLC. It is characterized by the rapid appearance of local and distant metastases or in the **lymph nodes**.

10-15%

- ***large cell carcinoma*** or anaplastic (poorly differentiated). It usually originates in the remoter areas of the lung and it has already a considerable size at the time of diagnosis. It has a worse prognosis than the two previous types and accounts for **10-15%** of all lung cancers.

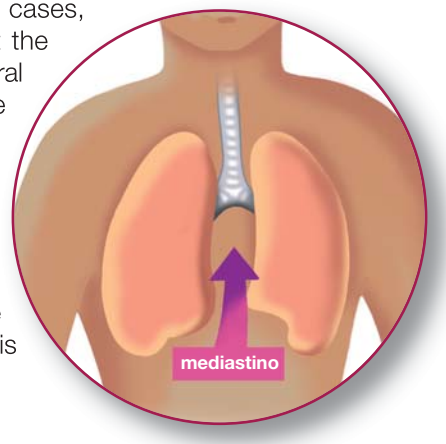
NSCLC: therapy

Each patient is considered and treated individually. The treatment choices depend on the type of disease (there are nowadays more appropriate treatments for certain types of non-small cell lung cancer), on its extension and on the patient general conditions and age. Early-stage lung cancer (ie confined to the lung, in the absence of locations elsewhere) is theoretically candidate for surgery resection and, when not possible for medical reasons, radiation therapy is the treatment choice. If the disease is localized at the lung, but with the involvement of **mediastinal** lymph nodes, then radiotherapy is used in combination with chemotherapy: the two treatments can be combined or sequentially administered. In the cases of metastatic disease, chemotherapy and targeted therapies can be used and radiation therapy may be useful for treating individual districts (such as bone and brain for example).

Small cell lung cancer (SCLC)

75%

Small cell lung cancer or microcytoma or 'oat cell' carcinoma, so defined due to the shape of its cells, is more aggressive than NSCLC and in **75%** of the cases, metastases are already present at the time of diagnosis. It often has a central origin and occupies that space between the two lungs called the mediastinum. It is characterised by a rapid growth and is more likely to spread to other organs and lymph nodes.



The risk of relapse (ie recovery of the disease after the end of treatment) is very high.

SCLC: therapy

SCLC spreads quickly so in the majority of the cases the most appropriate therapy is chemotherapy, which permits a disease systemic control.

In many cases, treatment also includes radiation therapy to shrink or destroy the primary tumor in the lung or tumors elsewhere in the body (such as in the brain). Some patients have radiation therapy to the brain even though no cancer is found there. This treatment, called prophylactic cranial irradiation or PCI, is given to prevent tumors from relapsing in the brain. Usually, PCI is reserved for patients whose lung tumor has responded well to treatment.

Surgery also can be part of the treatment plan for small cell lung cancer, but this treatment is appropriate only for a small number of patients.

4. Symptoms

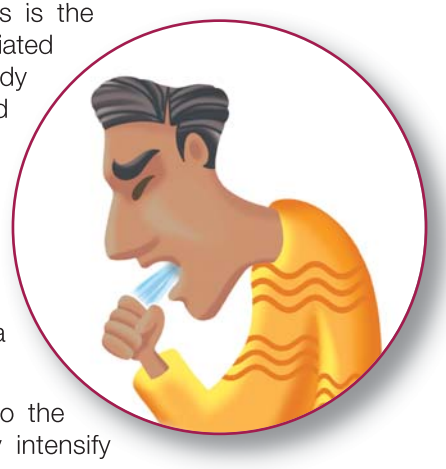
There are signals and disorders associated with the disease, which lead a person to go the doctor for a visit, starting in this way a process to get the diagnosis of a specific disease.

Lung cancer usually does not cause symptoms when it first develops. Doctors sometimes discover lung cancer in a person with no symptoms after the individual has a chest x-ray for another medical reason.

Usually, however, lung cancer is found after the growing tumor causes symptoms to appear.

Symptoms are often non specific and could be confused with those of other respiratory diseases.

- ***Cough.*** Productive or dry, this is the most common symptom associated with lung cancer. Since it is already present in most of smokers and in people suffering from chronic bronchitis, it is important to assess any changes in terms of intensity, duration and characteristics. For example, it may happen that rare coughing in the morning become a persistent cough during the day.



- ***Chest pain.*** Often radiating to the shoulder and the arm, it may intensify breathing and varying the position.
- ***Other symptoms.*** These may include: pneumonia and bronchitis with frequent relapses or difficult to treat, coughing up blood (haemoptysis), shortness of breath (dyspnea), hoarseness/lowering of the voice (dysphonia), face or neck swelling. There are maybe symptoms that do not seem to be related to the lungs. Like all cancers, lung cancer can cause unusual tiredness (asthenia), loss of appetite and loss of weight. When the cancer has spread to other body parts, depending on the organs you can have different symptoms such as headache, bone pain in one or more body sites, sclera (white of the eye) yellowing or the skin.

Other symptoms can be caused by substances made by lung cancer cells, entering the bloodstream can cause fever (especially in the evening), joint pain, value decrease of some blood tests (such as sodium). These disorders are classified as **paraneoplastic syndromes**.

Some symptoms may regress after starting the treatment, others are fading gradually. None of these symptoms is a sure sign of lung cancer; only a doctor can determine whether the symptoms reported are due to the cancer or to other problem.

5. Diagnosis

Lung cancer can grow for many years without causing any symptoms; for the majority of people, the diagnosis is not at onset of disease. A definition of a validated and efficacious **screening** for this tumor may anticipate the diagnosis. If lung cancer would be diagnosed before symptoms occur there would be more therapeutic options. At present there are not yet validated screening tests on a large scale (as already exist for breast and uterine cancer, for example). Beware therefore of tests that will be offered in private hospitals or that are not included in clinical trials approved by the Ministry of Health and make sure that are conducted in appropriate structures with a trained staff.

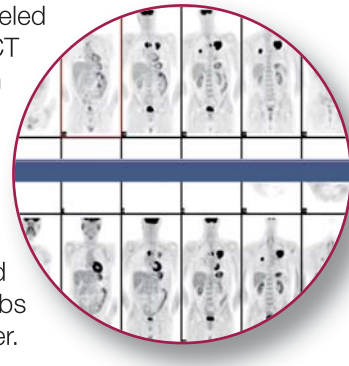
After the patient medical history and his objective examination (the patient visit), the doctor will prescribe to the person with symptoms, radiological, hematology (blood) and anatomopathological (the latter ones analyze the biological material collected during the diagnostic path) examination.

- ***Chest radiograph (chest x-ray).*** The chest radiograph is still one of the first tests performed for the identification of the disease. Its execution is very simple, quick and absolutely painless for the patient. But it does not allow to identify a small tumor or hidden behind a rib, the clavicle or the sternum area.

- ***Computed Tomography (CT) spiral.*** The CT scan has a greater sensitivity and specificity than the chest radiography (it is more precise) and more precision in defining the size, shape and the exact tumor location and its relationship with other structures in the chest. Usually it is done by adding a contrast agent (which can be drunk or injected into a vein), that makes it easier and more accurate the exam reading. With the first CT machines the examination lasted about 15-30 minutes; today, with the introduction of spiral CT, the radiological study of the chest lasts about 20-30 seconds, a short lasting time, and the patient can retain the breath, avoiding that the images appear disturbed by small body movements and also reducing the exposure to radiation. The CT study is then extended to the encephal and the upper abdomen, in order to assess the organs where lung cancer more frequently may produce metastases (liver, adrenal glands, brain). The CT is not able to provide the exact tumor nature, which needs the anatomopathological analysis, namely the search and description under a microscope of tumor cells on materials such as sputum, or liquid and tissue fragments taken with different techniques.

- ***Sputum cytology.*** It is the examination under a microscope of a sputum sample, the mucus expelled from the airways by coughing. It is likely that some tumor cells in the bronchi detach and are carried out through the sputum. The examination is simple, completely painless, and very rapid. The best time for collecting sample is in the morning, when secretions have accumulated in the airways during the prolonged supine position at night.

- ***Positron emission tomography (PET).*** In the PET the images are obtained after the intravenous administration of a substance (eg a sugar derivative) labeled with a radioisotope. It differs from the CT mainly because it can distinguish cancer cells - characterized by a high consumption of glucose (sugar), which favors their rapid growth and multiplication - than normal. Areas containing the cancer cells appear brighter on the PET images compared to normal tissues: it is like if small bulbs light up in body sites affected by cancer.

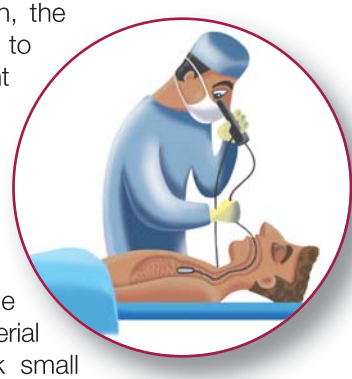


It is possible that the doctor gives an indication to perform this examination to better assess the extent of the disease. The exam is not painful and the execution requires about 3 hours and during at least 24 hours after this exam the patient must not stay close to pregnant women.

In some cases the doctor can give an indication to perform a **bone scan exam** (similar to PET, it assesses the skeletal system, ie the bones) or **brain magnetic resonance imaging** (MRI), which may be necessary in some cases for a better assessment of brain or spinal cord. Technically, MRI works like a CT scan, but within a structure (large tube) usually closed: if you suffer from claustrophobia, there are open machines (ask your doctor where you can find it).

- ***Cytological and histological diagnosis***

The **bronchoscopy** is the most common biopsy technique (ie sampling tissue) in a case of suspected lung cancer. Bronchoscopy permits to view directly the airways by the use of optic fibers. Passing through the nostrils or mouth, the bronchi are achieved and checked up to search possible anomalies. The outpatient bronchoscopy is performed after the administration of a small dose of local anesthetic to reduce the cough reflex. Various microscopic instruments can be inserted through bronchoscope, including tongs (to pick a small piece of tissue) or a toothbrush (to rub it inside the bronchial wall and to examine the material attached) or a small needle (to pick small amounts of tissue).



Sometimes another way may be more appropriate to get a small amount of tissue: the **CT-guided needle biopsy** of lung. This technique consists of inserting a needle through the chest wall to reach the tumor mass. This examination is practiced in the radiology department with a local anesthesia and with the guidance of CT. The patient lies on a bed of CT and the radiologist can see where it needs to direct the needle, guided by CT image.

If the CT examination describes the presence of pleural effusion (ie an increased production of fluid from the visceral pleural covering the lungs), the diagnosis can be made by examining this liquid. The procedure used by the doctor to obtain the liquid is called **thoracentesis**. This examination is done outpatient basis, using local anesthesia where the needle is inserted through the chest wall to extract the liquid.

In a few cases we must resort to surgical procedures to get a piece of tissue which might lead to a diagnosis. In these cases hospitalization is required (an average of 3 days) and a general anesthesia.

To better understand this moment, these are some questions you can ask your doctor:

- **Which methods has been selected in my case to reach a diagnosis? Why this?**
- **Is it painful? How long will I stay in the hospital?**
- **When will be available the results of the examination?**

6. Staging

Before statement of a correct therapeutic strategy it is essential to evaluate all the organs where the lung cancer may be present and the stage of it. This means studying the tumor extension and it is done by tests set out on pp. 12 and 13.

Small cell lung cancer is studied using the terms "limited disease" or "extended disease." The limited disease is localized in the chest, in the mediastinum and in the regional lymph nodes and it can be treated with radiation therapy (in combination with chemotherapy); the extended disease indicates the presence of distant metastases and is treated with chemotherapy.

The classification **of non-small cell lung cancer** is based on the TNM system: the letter T refers to the tumor size and the relationship with nearby organs; the letter N to the lymph node involvement and M to the metastases presence. The combination of T, N and M permit the doctor to identify the tumor's stage. The classification includes 4 stages, from I to IV stage.

Stadio I. The tumor has not spread to the lymph nodes or other organs and is still relatively small. This cancer is usually resectable.

Stadio II. The tumor has spread to the lymph nodes or into nearby tissues. Normally in this stage, the tumor can be surgically removed. It may require chemotherapy and/or radiation therapy combined (before or after) with surgery.

Stadio III. The tumor has spread within the chest and the mediastinal lymph nodes (or neck). Tumors in stage III are often not surgically treatable, but are undergoing chemotherapy and/or radiation therapy.

Stadio IV. The tumor is associated with metastases in other parts of the body. In this stage the best treatment is chemotherapy and nowadays there are also targeted therapies that can be added to standard therapies or administered alone. Even in this stage of the disease, radiation therapy may be required (for example, on a district level, such as bone or brain).

To better understand this moment, these are some questions you can ask your doctor:

- **What is the stage of the disease?**
- **What is (or what are) my treatments options? What is the goal of treatment?**
- **How long will therapy last? Can I do in an outpatient or should I be hospitalized?**
- **How will this treatment affect my daily life?**

7. Treatment options

The main treatment options currently used in lung cancer are surgery, radiation therapy, chemotherapy and targeted therapies, which can be used single or combined, depending on the type of cancer, the stage of disease and patient's age and general health.

Surgery. Surgery to remove the tumor is indicated in the early stages of the disease (ie when the cancer has not yet spread to other organs) and in patients with good general condition and pulmonary function.

Generally, the lymph nodes surrounding the tumor (ie those contained in the mediastinum) are removed with it, to verify that they are not already involved. The purpose consists in removing a lung lobe (lobectomy), two lobes (bilobectomia) or the entire lung (pneumonectomy). Before performing the surgery, the doctor and/or the surgeon make all the examinations necessary to assess whether **resection** is feasible, from a respiratory and cardiovascular point of view.

Surgery may be preceded or followed by chemotherapy or radiation therapy, to reduce the tumor mass (before surgery) or the risk of tumor relapse (after surgery).

These are questions you can ask your doctor if you are told that you are getting the surgery, to better understand your disease and to cope appropriately with it:

- **What kind of operation shall I have?**
- **How long must I stay in the hospital? Can I have back my lifestyle?**
- **What will I have to do in preparation for surgery or after surgery to improve the outcome? (ask suggestions for breathing exercises, important for post-operative recovery)**

Radiation therapy. This therapy uses high energy radiation to destroy or reduce the tumor mass minimizing the damage to healthy tissues. Radiation therapy can also play an important role in reducing pain, at any stage of the disease. Radiation therapy for lung cancer is often a combination therapy, with chemotherapy and/or surgery to reduce the tumor size before surgery, to increase the response of cancer cells to drug therapy and to reduce the possibility of local relapse of disease after surgical removal.

These are some questions you can ask your doctor if you are told that you are going to radiation therapy, to better understand your disease and to cope appropriately with it:

- **What is the purpose of radiation therapy in my case?**
- **How does radiation therapy work and how long for?**
- **How do I feel during radiation therapy treatment?**
- **What are the possible side effects and how can I face them and manage them?**

Chemotherapy. Chemotherapy uses anticancer drugs known as cytotoxic drugs, able to inhibite (blocking) the growth of cancer cells or destroy them. Chemotherapy is a systemic therapy (ie, it acts throughout the body) and is administered orally (by mouth) or, more commonly, by intravenous injection. Most chemotherapy drugs are administered in cycles, and with a specific timetable: many drugs used in lung cancer treatment are administered every 3 weeks, others have shorter time limits. These are the goals of chemotherapy in lung cancer: to reach a response that means stop or reverse the disease, to slow tumor growth and to prolong life, to prevent the spread of the tumor control symptoms associated with the disease. Even when chemotherapy does not lead to healing, a proper use can help people live longer and in better way.

Targeted therapies or biological drugs. This new class of drugs is able to identify and strike with perfectly and selectively the tumor cells by interfering with their ability to grow, multiply and spread, with minimal damage for healthy cells. These drugs used single or in combination with chemotherapy and are indicated in selected cases (ie they are part of what is called "personalized therapy").

These are some questions you can ask your doctor if you are told that you are going to chemotherapy, to better understand your disease and to cope appropriately with it:

- **What is the goal of chemotherapy in my case?**
- **What (or which) drugs are used and in what way (deadlines, duration of treatment)?**
- **What are the possible side effects and how can I face and manage them?**

8. Who will take care of you

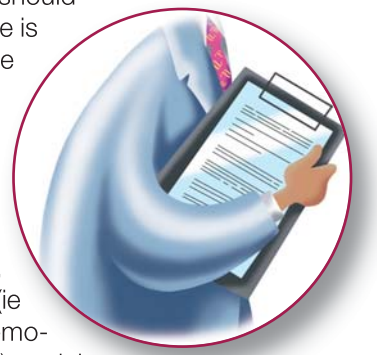
In the management of lung cancer various specialists are involved, with different roles depending on the type of disease. Among the most involved:

- ***Chest surgeon:*** is a surgeon more experienced in working the chest. In some countries this task is performed by cardiovascular surgeons. It is better to refer to a specialist with more experience in this field (rather than, for example, a general surgeon).
- ***Radiotherapist:*** who is in charge of radiation therapy. Not all hospitals have the equipment for radiation therapy, but your doctor will point you the appropriate structure and specialist.
- ***Pulmonologist:*** is a specialist who deals with respiratory diseases and is the person who performs bronchoscopy. In some countries (such as Italy for example) is the person who takes care of you if the prescribed treatment is chemotherapy.
- ***Oncologist:*** is the specialist who usually coordinates the treatment options, with the help of other specialists and is the person who will look after you if there is a need for chemotherapy.
- ***Psychologist:*** in a such difficult moment of a person's life, the support of a psychologist with oncology experience becomes very important to better deal with the disease and treatments. Many oncologist teams now have in their staff also a psychologist.
- ***Nurses:*** nursing staff has a relevant role in the disease, both in organizing the examinations that lead to diagnosis and during the treatment period.
- ***Medical analgesic therapy:*** your doctor will get help of a analgesic therapy service and doctors involved in pain treatment for an optimal pain control (if this occurs). Other specialists may be consulted for better managing your disease (such as orthopedics, neurology and others) and your doctor will give you the appropriate prescriptions.

After the diagnosis and before starting the treatment, it is important you are convinced that the doctor made and is still doing the best choice for you, this will allow you to deal better with the treatment. If you wish, you can ask a second opinion of another specialist, bringing with you all documentation relating to your disease. When you think you have achieved your inner confidence on the structure where you are in charge, start the therapy without wasting time on other visits, trips and advices. Remember that nowadays there are standardized diagnostic and therapeutic procedures worldwide, where experienced specialists in thoracic oncology should refer.

9. What is a clinical trial?

A clinical trial is a search mode through which new drugs and/or new therapeutic strategies are studied. You should know that any therapy doctors will propose is the result of a clinical study conducted in the past on people with your disease.



The participation in a clinical trial always helps the research to make progress, but it is important to have all the information about some studies evaluate a new drug in comparison with a standard therapy, other the administration mode of a drug (ie whether it is better to administer a chemotherapy every 15 days instead of every 28), mainly to improve their tolerability (ie to find a way that gives less side effects). There are studies that evaluate if the addition of a new drug to standard therapy may give better outcomes, others seeking the best dose of a new drug, and others evaluating the possibility of combining more drugs together, and so on. There are clinical trials for all types and stages of disease aiming to improve the control of the disease, to decrease the chances of relapse after the end of treatment, to reduce side effects of therapies, to personalize care (to give the most appropriate and less toxic medication to suitable person for that treatment).

You can ask your doctor if that structure offer one or more clinical studies to participate. In any case it is important you know what it is, how the treatment works, what the study purpose is and what it would be different from the standard therapy (ie not as part of a clinical trial). The clinical studies provide criteria for inclusion (ie the characteristics of the person and the disease that allow to join the study) and exclusion (ie the characteristics of the person and the disease that prevents them from joining the study): your doctor will verify if you are candidate for the specific study or not.

There are studies called "randomized", namely treatment decided (in the context of those provided by the study) random, so that you and/or the doctor lean towards one rather than another care. Before entering the study and after you have received all the information, you will be asked to sign an informed consent. It is still your right to decide to quit the trial (ie to stop that type of care) at any time, as the doctor may decide to let you quit the clinical trial if he/she believes that this is not the appropriate treatment for you (for lack of efficacy or excessive toxicity).

Before participating in a clinical trial these are the questions for your doctor to better understand and manage the disease:

- **What are the inclusion and exclusion criteria for this study? And considering them, am I a right candidates for it?**
- **What are the possible side effects of treatment that I am going to receive?**
- **What can it change for me to participate in this study, rather than follow a standard care? Shall I make additional tests?**
- **I know I can stop the clinical trial therapy at any time (or you can choose to do it for medical reasons): in this case what can you do for my disease?**

10. Glossary

Lymph nodes: structures of the lymphatic system filtering particulate as viruses, bacteria and cancer cells

Mediastine: area located in the chest center between the lungs; it contains the heart and major blood vessels entering and leaving the heart, trachea, esophagus, and many lymph nodes; mediastinal lymph nodes are often studied for the correct staging of lung cancer

Metastases: malignant cells that detach from the original tumor and spread to other organs where they reproduce and generate new tumors

Pleura: serous membrane covering the entire lung (visceral pleura) and the chest cavity (parietal pleura)

Resection: operation that aims to remove a tissue or part of an organ or a structure

Screening: tests periodically carried out in order to detect the presence of cancer before a person shows any symptoms

Paraneoplastic syndromes: signs and symptoms given by cancer far from the place where it develops. They occur after the production of substances that tumor cells enter into the circulation

WALCE Onlus (Women Against Lung Cancer in Europe)
is a non-profit organization created to make women aware
of the significant increase of lung cancer in women.
WALCE aims to spread knowledge of this disease in terms of prevention,
diagnosis and therapy.
WALCE was founded in 2006 as an Italian-Spanish initiative.
It aims to be the first association to function on a European scale
in the fight against lung cancer.
This is the disease which is difficult and complicated to treat and in which women
play a leading role on a daily basis, whether they are doctors, nurses, patients,
family members or caregivers.
Women are often a point of reference and a source of support and hope.

WALCE
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