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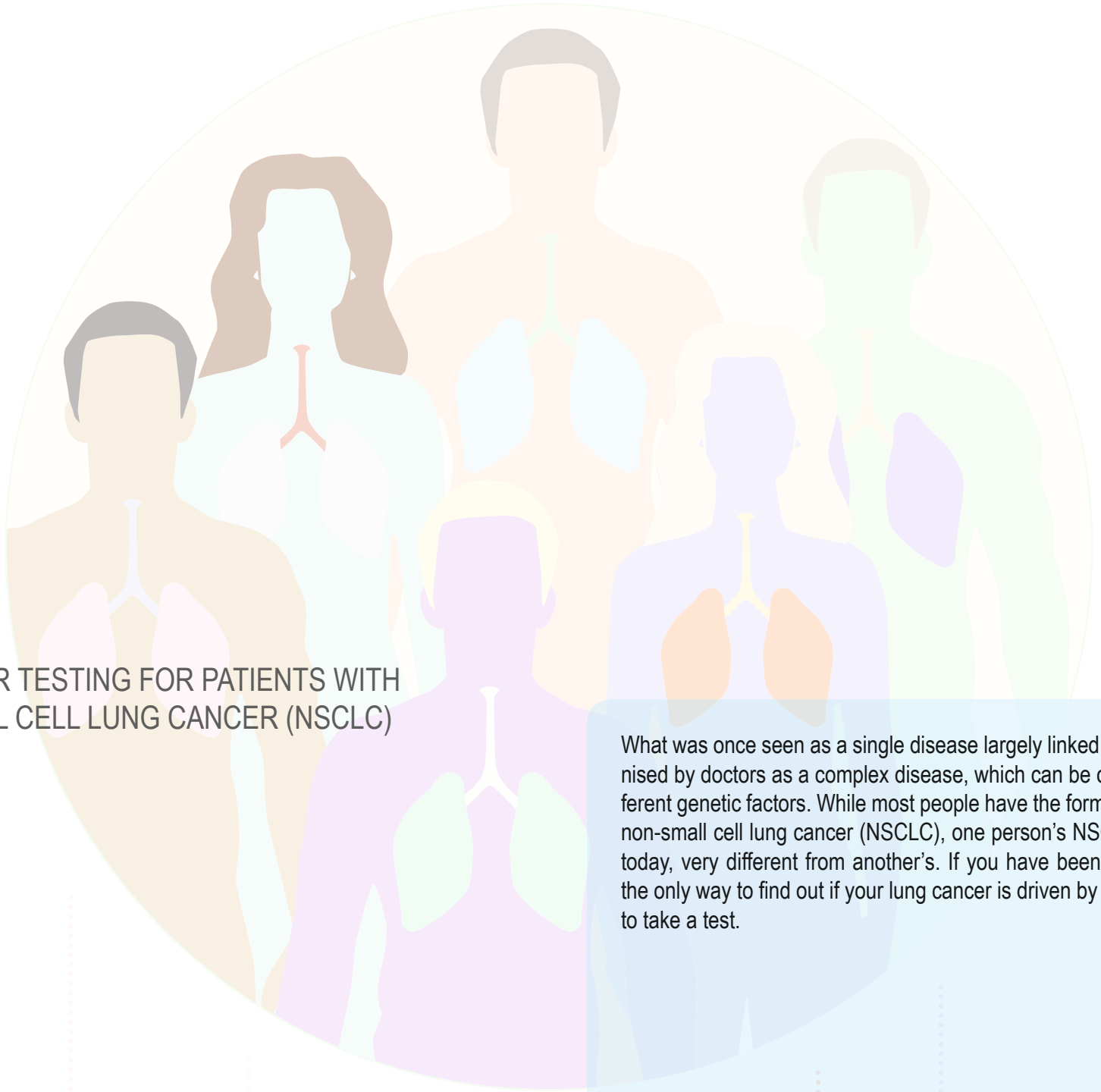
PROFILING LUNG CANCER

Molecular Testing for Patients with Non-Small Cell Lung Cancer (NSCLC)

Pfizer Oncology

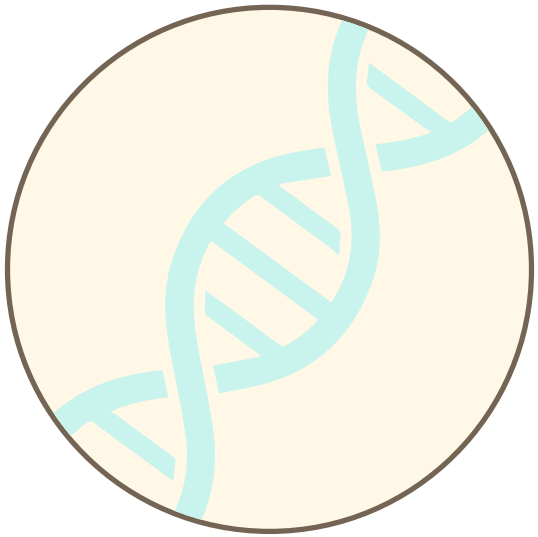
ROY CASTLE LUNG CANCER FOUNDATION

Lung Cancer Europe



MOLECULAR TESTING FOR PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC)

What was once seen as a single disease largely linked to smoking is now recognised by doctors as a complex disease, which can be caused by a variety of different genetic factors. While most people have the form of lung cancer known as non-small cell lung cancer (NSCLC), one person's NSCLC can be, as we know today, very different from another's. If you have been diagnosed with NSCLC, the only way to find out if your lung cancer is driven by a certain genetic factor is to take a test.



WHAT IS MOLECULAR TESTING?

Molecular testing looks at single genes or short lengths of DNA to identify genetic changes. In NSCLC it involves examining your tumour for specific molecules.[1] The presence of those molecules in your tumour tissue could reveal what is driving your cancer.

GENETIC CHANGES THAT MAY LEAD TO CANCER

Cells are the fundamental components of our body and work together to form our organs, including the lungs. Cancer starts with gene changes in one cell or a small group of cells. Due to these changes, faulty cells may start to grow and multiply too much and form a lump called tumour.

There are many reasons why 'healthy' cells can behave in this way:

- inherited gene changes within cells (mutations)
- exposure to certain substances or environments
- random chance with no outside cause (acquired mutations)

Acquired changes, in certain genes may make some lung cancers more likely to grow and spread than others. Not all lung cancers share the same gene changes, so there are undoubtedly potential changes that have not yet been identified.[2]

WHY SHOULD YOU BE TESTED?

Molecular testing helps your doctor to know what genetic change has caused your cells to be cancerous and to select the most appropriate treatment to target your cancer. This could lead to improved care and treatment outcomes.[3] Several targeted therapies are now available that are designed to fight specific features of tumours, including NSCLC.[4] Several more are still being developed in clinical trials evaluating their potential.

TARGETED THERAPIES – STOPPING GROWTH AND SPREAD OF CANCER

The knowledge of where certain genetic changes can occur has been used to develop new targeted therapies designed to block this process of tumour growth. There are various types of targeted therapies used for the treatment of NSCLC.[5] Each works in a different way to stop the growth and spread of the disease. At this time, they are most often used for advanced lung cancers, either along with chemotherapy or by themselves. To find out if a certain targeted therapy may be suitable for you, your doctor will perform molecular testing.

Most people experience some side effects from taking a targeted treatment, but these vary from person to person and depend on which drug you are taking.[6] It is important that you tell your oncologist or lung cancer nurse specialist if you are having problems.

CLINICAL TRIALS – ROUTE TO INVESTIGATIONAL TARGETED THERAPIES

Even if your tumour tests negative for genetic changes linked to approved targeted therapies, it may still test positive for other genetic characteristics that could allow you to take part in a clinical trial. Investigational targeted therapies for genetic changes are sometimes being tested in clinical trials, and treatments may be available to some patients through this route. To find out if a clinical trial may be suitable for you, ask your doctor and he will discuss with you the appropriate next steps.

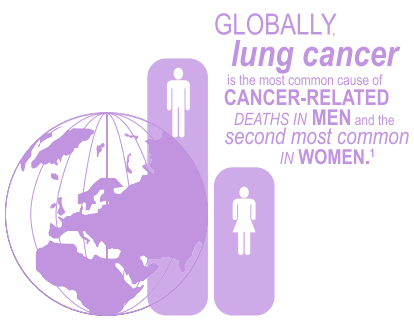
IMPROVING 'QUALITY OF LIFE'

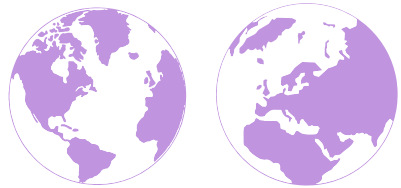
NSCLC and its treatment has a major impact on your life. Improving 'Quality of Life' (QoL) is thus an important goal during lung cancer treatment. Certain therapies may help enhance your QoL by alleviating symptoms, such as reducing coughing, making breathing easier and helping to reduce pain. Identifying the most appropriate treatment for your specific lung cancer is more likely to lead to an improved 'Quality of Life'.

WHO SHOULD BE TESTED?

To have as much information as possible about your lung cancer can be helpful so you and your multidisciplinary care team can work together to determine the best treatment plan for you – wether your cancer is potentially driven by a genetic change or not.

Therefore, it is recommended that all patients – smokers as well as non-smokers – with advanced non-squamous NSCLC, should be tested for all relevant genetic changes.[4,6] If you have NSCLC, molecular testing could give your doctors information that may guide your treatment plan or check your eligibility for clinical trials.[7,8] If you are not sure if you have been tested, you should ask your doctor.





NEW **LUNG CANCER** DIAGNOSIS
EACH YEAR:
& ABOUT **1.800.000** *worldwide*
410.220 *in Europe.*[2]

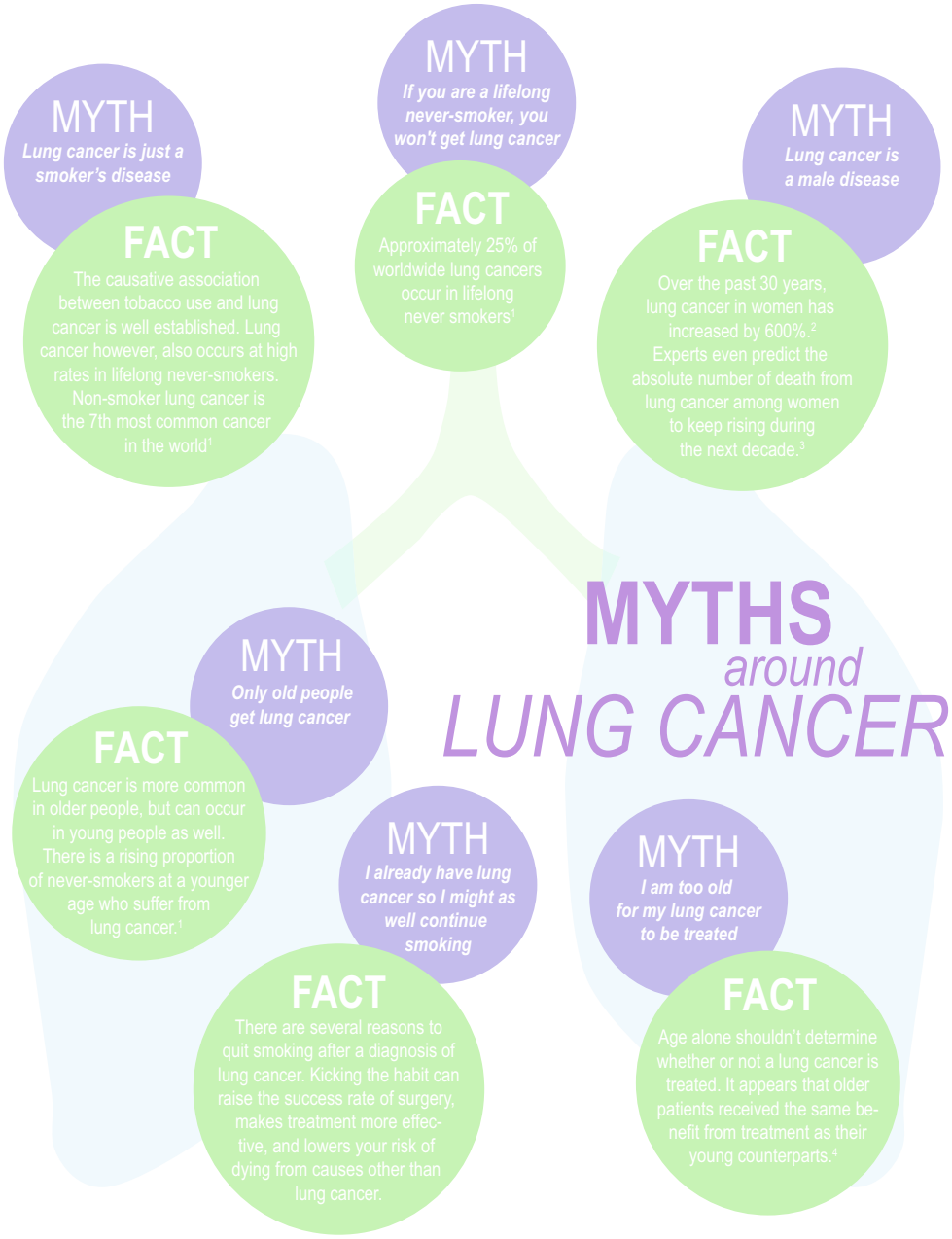
YOU ARE NOT ALONE

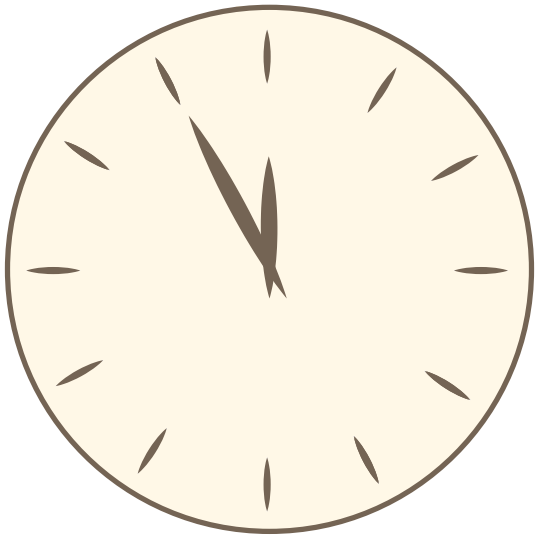
Many patients who smoke feel they are to blame for their cancer. If you feel stigmatised or judged because of your disease, and this is preventing you from asking for — or receiving — good care, you should speak with an organisation that supports and advocates for people living with lung cancer.

There are lung cancer communities across the world, online and in person, at national, local and regional levels. Each community contains compassionate and experienced cancer professionals, caregivers, and survivors.

MYTHS AROUND LUNG CANCER

Common myths and misconceptions about lung cancer include:





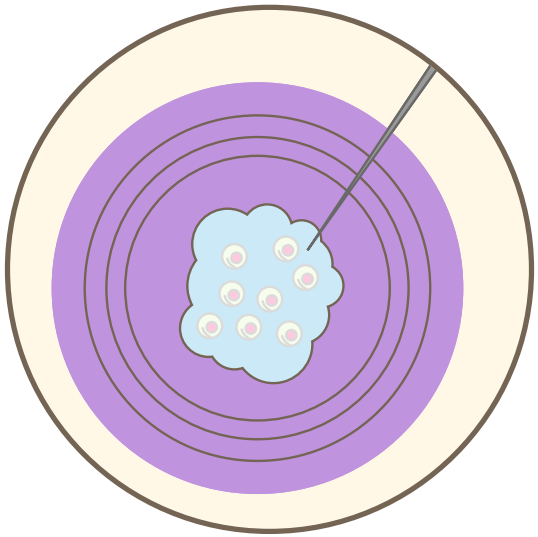
WHEN SHOULD YOU BE TESTED?

Getting the treatment tailored to your type of lung cancer is as important as getting it at the earliest moment possible. Renowned international medical societies and organisations recommend that molecular testing is carried out when you are initially diagnosed with advanced non-squamous NSCLC:[4,8]

Overview of medical societies and organisations that recommend molecular testing

- European Society for Medical Oncology
- College of American Pathologists
- International Association for the Study of Lung Cancer
- Association for Molecular Pathology

Patients whose disease has progressed from a lower stage disease and who have not previously been tested should also undergo testing. For these patients and those with advanced NSCLC, timely diagnosis can be critical in order to initiate the most appropriate treatment plan as soon as possible. For patients who are diagnosed with stage I, II, or III disease, testing is encouraged but the decision to proceed should be made collaboratively between the multidisciplinary care team and appropriate laboratory.[15]



WHAT IS TESTED?

Molecular testing involves examining your tumour for the presence of specific molecules, so called biomarkers. These distinctive fingerprints can reveal what is driving your cancer. Tests for these biomarkers are used to help detect, diagnose, and manage some types of cancer, usually in combination with other tests, such as biopsies. They may also be used to determine if the body is responding well to treatment for a disease or to monitor for recurrence. In NSCLC they help to detect what genetic change makes your cancer grow.

BIOMARKERS IN MOLECULAR TESTING

Amongst others, the identification of certain biomarkers during molecular testing means that patients have more treatment options available to them now than ever before. Personalised medicine is based on molecular testing, which has allowed our growing knowledge of biomarkers to identify targets for cancer treatments.[16]

KEY BIOMARKERS IN NSCLC

There are currently three known biomarkers, and potentially several more linked to non-squamous NSCLC. Testing for those genetic changes called EGFR, ALK and ROS1 are the most important molecular tests for you to undergo.[4,17]

- Epidermal Growth Factor Receptor (EGFR) – a gene involved in making cells grow and multiply. EGFR mutations are believed to cause cells to multiply more than normal. EGFR mutations are detected in nearly 50% of lung cancer cases in people who never smoked and in 12%–17% of NSCLC cases.[18]
- Anaplastic Lymphoma Kinase (ALK) – The Anaplastic Lymphoma Kinase (ALK) gene can be found in everyone's DNA. Sometimes the ALK gene can attach to another gene and change the way each gene normally functions. This is called an ALK gene rearrangement and can contribute to cancer-cell growth and tumour survival in around 3%–5% of NSCLC tumours.[1,18]
- ROS1 – The ROS1 gene can also be found in everyone's DNA. Sometimes the ROS1 gene can attach to another gene and change the way each gene normally functions. This is called a ROS1 gene rearrangement and can contribute to cancer-cell growth and tumour survival in approximately 1%–2% of patients with NSCLC.[16,17]

HOW IS THE TUMOUR TESTED?

NSCLC-biomarkers are found in tumour tissues. Hence, the first step in getting a molecular test is collecting an adequate amount of tissue from your tumour. This is called a biopsy. Ideally, there is enough tissue remaining from your first tumour biopsy. If not, you may need a second one. The sample of your tumour tissue will be tested for all relevant biomarkers that potentially make your tumour grow. If any of these are missed, it could limit possible treatment options. There are dedicated tests for identifying biomarkers linked to your cancer. They will be carried out in a specialised laboratory. Your doctor should receive the results of the test within 10 working days.

TISSUE COLLECTION – QUALITY AND REQUIREMENTS

The accuracy of molecular tests depends on the quality of the tissue sample as much as the molecular analyses themselves, emphasising the importance of good sample collection and proper processing techniques.[19] Due to the increasing number of molecular tests that should be performed on samples from NSCLC patients, tissue sample size should be maximised whenever possible.[22]

NEED FOR BIOPSIES

The diagnosis of lung cancer is based on the careful examination of tissue taken during the biopsy of a suspected tumour. The tissue sample is examined by a pathologist to see if cancer cells are present and, if so, to find out the type of cancer.

The pathologist will also record the size and location of the tumour, the number of lymph nodes containing cancer cells and other important facts about the cancer.

The examination of biopsy samples offers the most valuable information for the diagnosing and staging of lung cancer. There are several ways of carrying out a biopsy – the method used by your doctor depends on where the sample will be taken from and your overall health. Some biopsies can be performed without needing an overnight stay in hospital.

NEED FOR REBIOPSIES

In some cases, the pathologist may not be able to identify the type of cancer during the first biopsy, because the tissue sample is too small or in poor condition. When this happens, another biopsy may be necessary.

A patient's cancer may alter or progress following initial treatment. In this case, a rebiopsy may be required, to assess how the cancer has developed. This is especially useful in the treatment of NSCLC, where another biopsy can provide an updated overview of the tumour's characteristics and may suggest an alternative targeted therapy.[20] In some patients whose cancer is as a result of a specific genetic change, the tumour may become resistant to targeted therapy. [22]

BIOPSY RESEARCH

Biopsies are essential to provide an accurate cancer diagnosis. However, there are certain scenarios in which a regular biopsy is not possible, presenting a significant challenge for doctors. Some patients may not be candidates because of poor health or because of a tumour's location in the body. Researchers are investigating new procedures to overcome these barriers, such as liquid biopsies. These are non-invasive blood tests that detect tumour cells and fragments of tumour DNA that have entered the bloodstream.

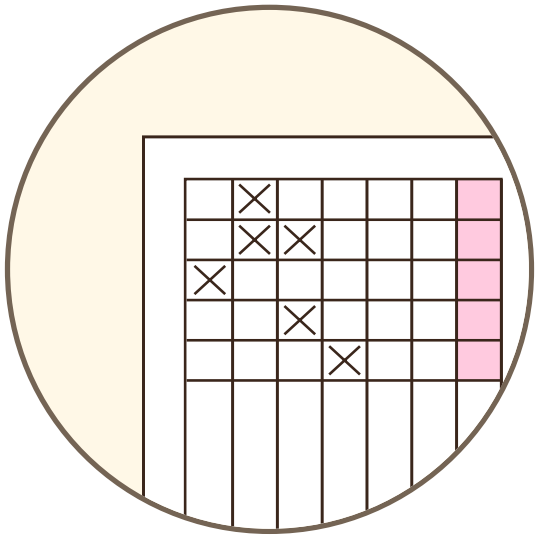
WHAT ARE THE BENEFITS AND LIMITATIONS OF MOLECULAR TESTING?

Knowing what drives your cancer can bring a sense of relief after a period of uncertainty. While testing has the potential to generate feelings of anger, anxiety or guilt regarding the results, especially when family members may be impacted, a healthcare professional should explain in detail the benefits, risks, and limitations of a particular test. It is important that you understand all of the potential outcomes of molecular testing before deciding to proceed.

While molecular testing does not provide a cure, it has become fundamentally important in helping specialists to understand your tumour and ultimately to choose the most effective and safe treatment option for you.

About half of NSCLCs are linked to known biomarkers. However, targeted therapies have not yet been identified for all of them. A molecular test can tell your doctor which of the known genetic changes may be driving your NSCLC, as well as which are not.

Some people with NSCLC will test positive for a tumour driven by a biomarker that may be treatable with a currently available targeted therapy. Others may test positive for a biomarker that may make them eligible for a clinical trial. Still others may not test positive for any biomarkers at all. However, if your tumour has no known qualities that can be matched to a targeted treatment, there are other suitable treatment options for you. Discuss with your doctor how the right treatment pathway for you could look.



AFTER TESTING: TREATMENT & CARE OPTIONS

If you test positive for known biomarker that makes your tumour grow, you may benefit from a currently available targeted therapy.7 Your doctors will examine the results of the test and decide on the most appropriate course of action.

PLANNING THE TREATMENT

At all stages of lung cancer diagnosis, a variety of tests are required in order to determine the most appropriate treatment for you. Apart from the initial biopsy and molecular testing, these include:

- A report of your health history and examination of your body
- Blood tests
- CT scans of the insides of your chest and belly area

Depending on the stage of the diagnosis, additional tests may also be recommended, such as MRI scans, lymph node tests and checking of the lung function.24 It may also be appropriate to seek a second opinion from another pathologist with extensive expertise in interpreting lung cancers if the pathology report does not contain a definite diagnosis, if you have a rare type of cancer or if the cancer has already spread. Another pathologist's interpretation can confirm your diagnosis or may suggest an alternative diagnosis.

TREATMENT OPTIONS

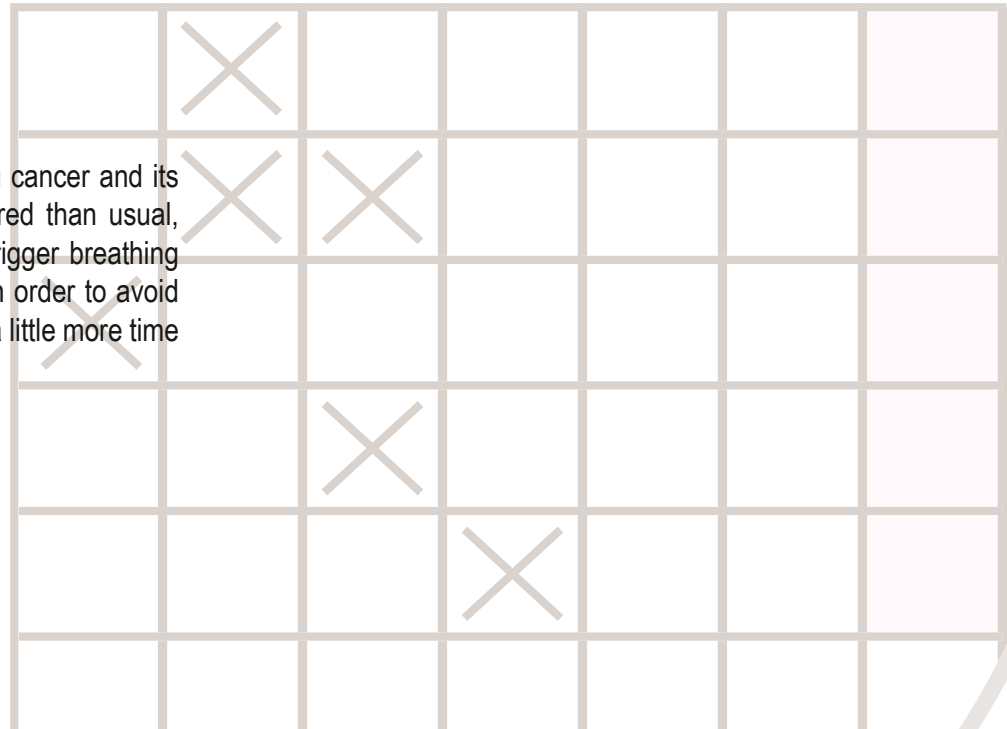
Treatment options vary depending on the stage of the cancer, in addition to its size, position in the lung and whether it has spread to other parts of the body. But your overall health and lung function, as well as certain traits of the cancer itself, are also important.

For example, Stage IV or advanced NSCLC is widespread when it is diagnosed, making it very hard to cure. In this case, treatment options depend on where the cancer has spread to, the number of tumours, and your overall health. If you are in otherwise good health, treatments such as surgery, chemotherapy, targeted therapy, immunotherapy or radiation therapy may help you live longer and improve your quality of life by relieving symptoms. It is important to understand the goals of the treatment before you start.

LIVING WITH LUNG CANCER

Every patient will have a different experience of living with lung cancer and its impact on their daily life will be unique. You may feel more tired than usual, particularly while undergoing treatment.5 Some activities can trigger breathing difficulties and you may need to alter your day-to-day routine in order to avoid this.5 It is important to take things at your own pace and to take a little more time to plan your approach to your day.

Following treatment, you may want to think carefully about your priorities with regards to family, work and your routine. Returning to your life exactly as it was prior to your diagnosis might not be appealing, or possible. Taking each day at a time will help you to adjust and to work out your next steps.



Disclaimer

This brochure is developed for patients, their families and the general public, to help them navigate molecular testing. The brochure has a particular focus on NSCLC, the most common form of lung cancer.The brochure is to be used for informational purposes only. This document is not a substitute for medical advice or for the opinion of a health care provider. You should always consult a doctor or nurse if you have any questions regarding the information set out in this document. All of the steps outlined in the molecular testing brochure are subject to clinical judgment and your journey may not follow the proposed steps set out within. This information does not create a doctor-patient relationship between Pfizer and you.