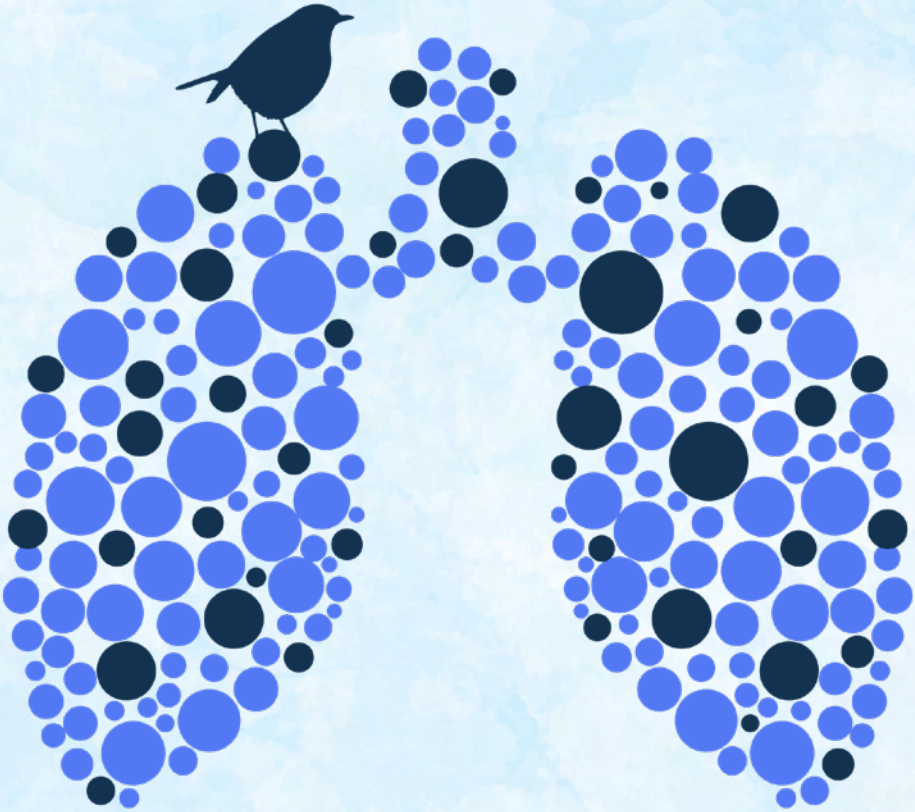
RUTH STRAUSS FOUNDATION

NON-SMOKING LUNG CANCER INFORMATION



ANYONE WITH LUNGS CAN GET LUNG CANCER

CONTENTS

INTRODUCTION

If you have been diagnosed with lung cancer and you have never smoked, it can be overwhelming and hard to make sense of. This booklet is here to help you feel more informed, more confident and clearer about what questions to ask next.

Lung cancer is the fourth most common type of cancer in the UK. It's well known that current and ex-smokers are most at risk, but non-smokers can also get lung cancer. As many as 1 in 4 lung cancer cases occur in non-smokers.

At the Ruth Strauss Foundation, we aim to raise awareness of non-smoking lung cancers. Alongside awareness-raising campaigns, we fund research to help improve early diagnosis and ensure people affected by non-smoking lung cancer receive the best possible care.

We also offer guidance and support for parents with dependent children facing any incurable cancer. We help parents talk openly with their children about their cancer and its impact on their family.

In this booklet, we use the term 'non-smoker' for people who've never smoked or have smoked fewer than 100 cigarettes in their life.

We also use the term 'non-smoking lung cancer' to describe the type of lung cancer that typically affects non-smokers.

The aim of this booklet is to help you understand more about non-smoking lung cancer, the treatment options available, and how your care may be planned. We hope it will help you feel informed and confident in asking questions and advocating for yourself, so you can receive the best possible care - whatever the stage of your cancer.

For further support and information, visit **ruthstraussfoundation.com**

WHAT IS CANCER?

Medical language can feel overwhelming - especially at the start. This section explains the basics in plain terms, so you can understand what your doctors mean.

Cancer occurs when something in our cells goes wrong and they keep growing out of control.

Normally, the way our cells act is controlled by our genes. Our genes are rather like computer programs - they instruct our cells how to grow and behave. Genes are made of short strands of DNA that contain all the information cells need to make proteins. Proteins are tiny complex molecules that are involved in nearly every process in the body.

Sometimes the DNA in our genes gets damaged. Often our cells can detect this damage and repair it. If a cell cannot repair the damage to the DNA, it will usually self-destruct. This is a natural process called apoptosis - it helps to keep our bodies healthy.

Cancer happens when the damaged DNA in a cell isn't repaired properly and the cell doesn't self-destruct. The gene with the damaged DNA is now said to have a 'mutation'.

When genes get damaged, they can cause cells to make abnormal proteins that affect cell growth. In cancer, cells grow and divide too fast and as time passes, they form a lump or tumour.

A tumour is only cancerous (malignant) if it's able to spread to other parts of the body. Tumours that cannot spread are non-cancerous or benign.

WHAT IS LUNG CANCER?

WHAT DOES IT MEAN TO HAVE LUNG CANCER?

Lung cancer is defined by where it starts. Cancer that begins in the lungs is called primary lung cancer. Cancer that spreads to the lungs from another part of the body is known as secondary lung cancer.

There are two main types of primary lung cancer:

- **Non-small cell lung cancer (NSCLC)** - around 80-85% of cases
- **Small cell lung cancer (SCLC)** - around 15% of cases and rare in non-smokers

LUNG CANCER IN NON-SMOKERS

What type of lung cancer do non-smokers usually have?

Most non-smokers diagnosed with lung cancer have non-small cell lung cancer. Within this group, there are two main subtypes:

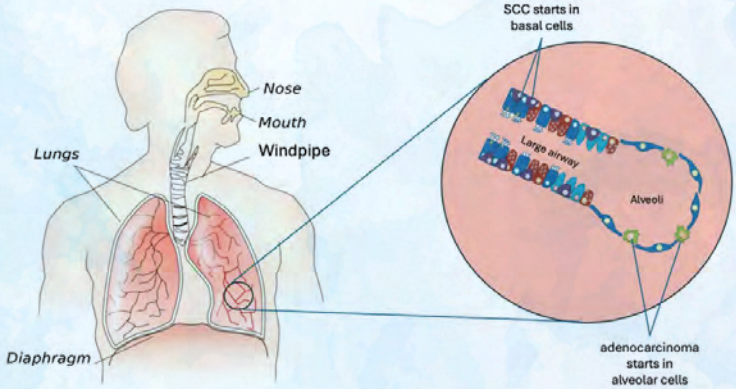
Adenocarcinoma

This develops in alveolar cells, which line the tiny air sacs (alveoli) in the lungs where oxygen passes into the blood. It is the most common type of lung cancer seen in non-smokers.

Squamous cell carcinoma (SCC)

This develops in basal cells, which line the larger airways of the lungs.

Understanding the type and subtype of lung cancer is important because it helps guide treatment decisions.



Adapted from Vickers (2018), *Cancer Biology & Treatments.*

WHY DO NON-SMOKERS GET LUNG CANCER?

It's not always possible to find the exact cause of a non-smoker's lung cancer. However, there are well-known factors that, alone or together, can increase a person's risk of getting lung cancer.

AIR POLLUTION

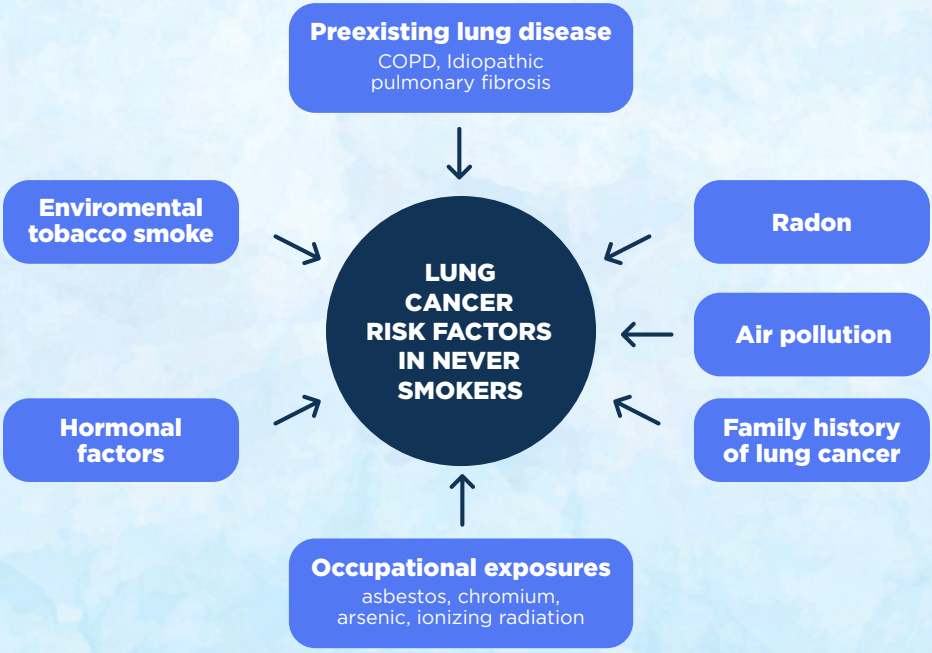
Research has found a link between air pollution and lung cancer. Long -term exposure to air pollution increases a person's risk of getting lung cancer.

PASSIVE SMOKING

As many as 1 in 3 non-smoking lung cancers may be due to second-hand smoke. The longer you spend in the close company of smokers the greater your risk. Research suggests that being exposed to second-hand smoke when young (under 25 years) poses the greatest risk.

LUNG DISEASE

People with a history of pneumonia or COPD are thought to be at higher risk of lung cancer. Also, infections such as tuberculosis and HPV have been linked to a greater risk of lung cancer.



RADON GAS

Radon is a colourless and odourless gas that is known to increase the risk of lung cancer. Radon is found in soil and rocks. Over time it can seep into the foundations of buildings. However, for most people in the UK, the risk of being exposed to dangerous levels of radon is low.

ASBESTOS

Asbestos is a material that was once used in buildings. It's now well known that it can cause lung cancer and so its use has been banned. However, people working in the building trade may still come into contact with asbestos, which increases their risk of lung cancer.

CHEMICALS AND RADIATION

The risk of lung cancer increases with exposure to arsenic, chromium or radiation.

People who do certain types of work are more likely to be exposed to these risk factors. These include miners, steel workers and people who work with wood preservers or pesticides.

FAMILY HISTORY

The risk of lung cancer is greater for people with a close relative (parent, sister or brother) who have also had the disease before the age of 50. This risk is also higher for people with a close relative who has been diagnosed with adenocarcinoma. The reason for this increased risk is not always clear. It may be due to shared genes. Or it could be because of living together and being exposed to the same risk factors.

WHY MIGHT LUNG CANCER DEVELOP IF YOU HAVE NEVER SMOKED?

Watch a short animation explaining why lung cancer can develop in people who have never smoked. It may help you and your family make sense of what can feel like an unexpected diagnosis.

To watch, visit **ruthstraussfoundation.com/NSLC-videos**

HOW IS LUNG CANCER DIAGNOSED?

Diagnosis often begins after symptoms prompt a GP visit, though sometimes lung cancer is found during tests for another condition.

WHAT SYMPTOMS MIGHT OCCUR?

Lung cancer symptoms are the same for smokers and non-smokers. They can include:

- A cough that has gone on for 3 weeks or more
- A long-term cough that has got worse
- Persistent or worsening back or shoulder pain
- A tight or painful chest
- Repeated chest infections
- Coughing up blood
- Ache or pain when coughing or breathing
- Feeling breathless
- Poor appetite
- Losing weight without meaning to
- Feeling tired

You might have one or more of the above symptoms. In the early stages of lung cancer, it's possible to have no symptoms.

If your GP suspects lung cancer they will send you for further tests, or they may refer you directly to a hospital specialist.

WHAT TESTS ARE USED?

There are a number of tests doctors can conduct to see if you have lung cancer. These include:

Chest X-ray

A chest X-ray will show the size and position of a cancer. It can also show if the cancer has begun to spread.

CT scan

A computerised tomography (CT) scan uses X-rays. However, unlike a flat X-ray, a CT scan creates a far more detailed 3-D image of inside the body.

PET scan

Cancer cells tend to use more energy and be more active than normal cells. This key difference can be seen with a positron emission tomography (PET) scan.

For a PET scan you will be injected with a mild radioactive sugar dye. The amount of radiation in the dye is small, about the same as a standard X-ray.

As cancer cells require more energy than other cells, they absorb more of the sugar dye. This makes them visible to the PET scanner.

MRI scan

A magnetic resonance imaging (MRI) scan uses strong magnets and radio waves to provide detailed images of the inside of the body.

Tissue biopsy

Cancer cells tend to look and behave differently from normal cells. To examine these differences, doctors need to remove a small tissue sample from the suspected tumour. This process is called a biopsy.

Doctors look at the sample under a microscope to see if cancer cells are present. Tissue samples may also be used to conduct other tests, such as molecular testing. The results of a biopsy are very helpful for making treatment choices.

There are a number of different ways a biopsy can be done:

- Needle biopsy. This involves inserting a long hollow needle through the skin to obtain the tissue sample. The process can be guided with X-ray, ultrasound, CT or MRI scans.
- Surgical biopsy. This is where a tissue sample is removed during surgery.
- A bronchoscope biopsy. This involves inserting a thin, flexible tube into the lung. The tube has a tiny camera for guidance and so doctors can see what tissue to take.

Liquid biopsy

As a tumour grows, bits of it can break off into the bloodstream. A liquid biopsy is a blood test that can detect cancer cells and/or fragments of tumour DNA called circulating tumour DNA (ctDNA). Liquid biopsies are quite new, but they are being used more and more to test for lung cancer. All people suspected of stage 3 or 4 non-small cell lung cancer should be offered a liquid biopsy.

DID YOU KNOW?

It's completely normal to feel overwhelmed at this stage. You do not need to absorb everything at once.

"...once a cancer diagnosis is made, further steps need to be taken to find out more about your cancer. For non-smoking lung cancers, it is vital that a biopsy is taken and sent off for molecular testing."
- Professor Sanjay Popat, RSF Scientific Advisor

UNDERSTANDING THE STAGE OF YOUR CANCER

WHAT DOES "STAGE" MEAN?

Doctors use **staging** to describe how large a cancer is and how far it has spread. There are four main cancer stages (1-4), which give an overall picture of the disease.

To determine the stage, doctors use the TNM system, which looks at:

- **T (Tumour):** the size and position of the tumour
- **N (Nodes):** whether cancer has spread to nearby lymph nodes
- **M (Metastasis):** whether cancer has spread to other parts of the body

The individual TNM findings are then combined to assign an overall stage from 1 (early, localised cancer) to 4 (advanced cancer that has spread to distant parts of the body).

THERE ARE FOUR MAIN STAGES:

Stage 1

The tumour is no larger than 4 cm in size. The cancer has not spread to the lymph nodes or outside the lungs. Stage 1 lung cancer is also known as 'localised or early cancer'.

Stage 2

The tumour can be up to 7 cm in size. The cancer may have spread to nearby lymph nodes, other parts of the lung or just outside the lung. Stage 2 lung cancer is also known as 'locally advanced cancer'.

Stage 3

The tumour can be any size, but it has begun to spread locally or is larger than 7 cm. It may have spread to:

- Other parts of the lung.
- Further away lymph nodes (such as those in the neck, or those near the opposite lung).
- Tissues that surround the lungs, such as the food pipe (oesophagus), the windpipe (trachea), or the heart.

Stage 3 lung cancer is also known as 'locally advanced cancer'.

Stage 4

The tumour can be any size and may have spread to:

- The other lung or nearby structures.
- Lymph nodes further away. Another part of the body, such as the liver, bones, brain, or other organs. Stage 4 lung cancer is known as ‘metastatic or advanced cancer’.

Stage 4 disease may be widespread, or it may be oligometastatic. The term “oligometastatic” is used when the cancer has gone beyond local spread but there is no agreed definition of the number of lesions that oligometastatic covers, but one study suggests between 1 and 5 lesions in the body.

My notes

THE IMPORTANCE OF MOLECULAR TESTING

Why is molecular testing so important?

After diagnosis and staging, doctors need to understand what is driving the cancer at a genetic level. Molecular testing looks for changes (or mutations) in DNA, genes, proteins and other molecules. These changes can help doctors decide the best treatment for you.

What is molecular profiling?

As you read in this booklet, some gene changes can cause cancer. These are called 'driver mutations.' Driver mutations often happen in genes that play a role in cell growth and survival. When these genes change, the proteins they make can become too active or stop working properly.

Knowing whether your cancer has a driver mutation can help to guide your treatment choices. In the UK, every person with lung cancer can have full molecular testing through the NHS.

DID YOU KNOW?

A biopsy is when a small piece of the tumour is removed for analysis, to be able to:

1. Confirm the cancer type
2. Identify the abnormal gene behind the cancer

WHERE YOUR BIOPSY SAMPLE IS ANALYSED

Your lung cancer biopsy sample will be sent to one of the 12 Genomic Laboratory Hubs (GLH) in the UK. These are:

England:

- Central and South West, led by Birmingham Women's and Children NHS Foundation Trust.
- East, led by Cambridge University Hospitals NHS Foundation Trust.
- North West, led by Manchester University NHS Foundation Trust.
- North Thames, led by Great Ormond Street Hospital for Children NHS Foundation Trust.
- South East, led by Guy's and St Thomas' NHS Foundation Trust.
- South West, led by North Bristol NHS Trust.
- North East, led by The Newcastle upon Tyne Hospitals NHS Foundation Trust.

Scotland:

- NHS Grampian, Aberdeen.
- NHS Tayside, Dundee.
- NHS Lothian, Edinburgh.
- NHS Greater Glasgow & Clyde, Glasgow.

Wales:

- All Wales Medical Genomics Service.

WHAT GENETIC CHANGES MIGHT BE FOUND?

This section introduces some of the genetic changes that are more commonly found in non-smoking lung cancer. You do not need to understand all of these in detail - what matters most is knowing whether any apply to you, as this can influence your treatment options.

Identifying a mutation can open the door to targeted therapies designed specifically for that cancer type.

There are 8 key genes in non-smoking lung cancer, where driver mutations are known to occur. The data is from worldwide studies:

- **EGFR** stands for epidermal growth factor receptor. It's a protein that sits on the surface of cells and is involved with cell growth. Changes to the EGFR gene can mean that cells make too much EGFR protein, which leads to higher cell division. Between 30-54% of non-smoking lung cancers are EGFR-positive.
- **ALK** is a protein involved in cell growth and survival. The ALK gene can break and fuse with another gene (usually one called ELM-4). This results in an abnormal ALK protein that may cause cells to keep dividing. Between 2.4-14% of non-smoking lung cancers are ALK-positive.
- **KRAS** is a protein involved in passing growth signals from outside a cell to the inside. Changes to the KRAS gene can cause cells to keep growing and spread throughout the body. Between 6-13% of non-smoking lung cancers are KRAS-positive.
- **BRAF** is a protein involved in sending cell messages, cell growth and cell survival. Changes to the BRAF gene can lead to uncontrolled cell growth and division. Between 3-12% of non-smoking lung cancers are BRAF-positive.
- **MET** is a protein essential for cell survival and function. Changes to the MET gene can lead to uncontrolled cell growth and spread. Between 2.8-10% of non-smoking lung cancers are MET exon 14 skipping.

- **HER2** (ERBB2) stands for human epidermal growth factor receptor 2. HER2 proteins sit on the surface of cells and help control normal cell growth. Changes to the ERBB2 gene can cause more HER2 protein to be produced. This can lead to cancer cells growing more quickly and spreading to other parts of the body. Between 3-5% of non-smoking lung cancers are HER2-positive.
- **ROS1** is a protein involved in sending cell signals and controlling cell growth. Similar to the ALK gene, the ROS1 gene can fuse with other genes, resulting in a protein that promotes uncontrolled growth of cancer cells. 3% of non-smoking lung cancers are ROS1-positive.
- **RET** is a protein normally involved in cell growth and the development of nerve cells. Changes to the RET gene can encourage abnormal cells, such as cancer cells, to grow. Up to 3% of non-smoking lung cancers are RET-positive.

"For never-smoker patients with stage 4 disease, I always say we have got to wait for the molecular results to come through - unless it's an emergency, in which case we start treatment with chemotherapy. Waiting for the molecular test results to come through will really help us work out what the right treatment for you is, and there's a very high likelihood that you will need molecular targeted therapy (TKI)."

TREATMENTS FOR NON-SMOKING LUNG CANCER

What treatments might be recommended?

Treatment is planned by a multidisciplinary team (MDT) and depends on cancer type, stage, molecular profile and overall health.

The treatment your team recommends will depend upon a number of factors, including:

- Your type of lung cancer.
- The results of molecular testing.
- The position and size of your cancer.
- The stage of your cancer.
- Your overall health.

The most common treatments for non-smoking lung cancer are:

- Targeted treatment.
- Surgery.
- Chemotherapy.
- Radiotherapy.
- Immunotherapy.

You may be offered one or a combination of these treatments.

WHY IS TESTING YOUR CANCER IMPORTANT?

Effective treatment depends on understanding the specific type and genetic profile of your cancer. This short animation explains why tests such as tissue biopsies and blood tests are essential before treatment begins, and how they help guide your care.

To watch, visit ruthstraussfoundation.com/NSLC-videos

UNDERSTANDING YOUR TREATMENT OPTIONS

Targeted treatments

If molecular testing finds a driver mutation in your cancer, there might be a specific treatment that can block the proteins linked to it. These are called targeted treatments, and they are very often used to treat people with non-smoking lung cancer. Targeted treatments have the added benefit of being tablets, so you can take them at home. To find out if a targeted treatment could help you, you must have had full molecular testing.

Currently, there are treatments that target:

- EGFR-positive lung cancer.
- ALK-positive lung cancer.
- ROS1-positive lung cancer.
- KRAS G12C-positive lung cancer.
- MET exon 14 skipping positive lung cancer.
- RET-positive lung cancer.

Although there may not be a targeted treatment available for your type of lung cancer, many new drugs are being studied in clinical trials. These include treatments for the following driver mutations: MET, KRAS, BRAF and ROS1. You may be able to join one of these trials. Ask your doctor if they know of any trials that might be right for your kind of cancer.

Surgery

Surgery may be an option if your cancer is detected early and is not yet widespread. Having surgery will depend on whether you are fit enough and if it's possible to remove the tumour. There are 3 main types of surgery for lung cancer:

- Wedge resection - a small piece of the lung is removed.
- Lobectomy - a large part of the lung (lobe) is removed.
- Pneumonectomy - the entire lung is removed.

Chemotherapy

Chemotherapy targets fast-growing cells. As cancer cells grow and divide far quicker than most normal cells, chemotherapy is used to kill or halt the growth of cancer. Generally, there are two reasons why chemotherapy is used:

- To cure the cancer, reduce the chance of it returning or slow its growth.
- To reduce the size of tumour to ease symptoms.

There are many different types of chemotherapy drugs. They can be used alone or together. You might also be offered chemotherapy with radiotherapy. This is called chemoradiation.

Chemotherapy may also be part of your treatment plan, together with surgery. It can be given before surgery to help shrink the tumour (called neoadjuvant chemotherapy) or after surgery to reduce the risk of the cancer coming back (called adjuvant chemotherapy).

Radiotherapy

Radiotherapy uses radiation to kill cancer cells. There are several ways radiotherapy is given to people with lung cancer:

- Radical radiotherapy. This is an intense course of treatment that may be used if you are not able to have surgery. This treatment often aims to get rid of/treat the cancer.
- Stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) are a very precise type of radiotherapy that is used instead of surgery. Both are the same type of treatment, and the terms are used interchangeably. SBRT or SABR accurately delivers high doses of radiotherapy, often in just a few sessions. It's useful for small cancers or when the cancer is in a difficult place in the body.
- Palliative radiotherapy. This is used to ease symptoms and slow the spread of cancer when a cure is not possible.
- Prophylactic cranial irradiation (PCI). This is a type of brain radiotherapy that is often given to people with certain types of lung cancer. It's a preventive treatment designed to stop cancer spreading to the brain - even if there are no signs of cancer there yet.
- Whole brain radiation (WBRT). This treatment is given when cancer has already spread to the brain. It delivers radiation to the entire brain to relieve symptoms and slow the growth of the cancer.

Gamma Knife

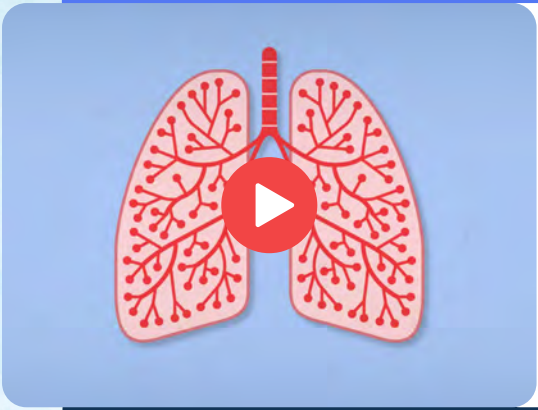
This treatment is used when there is one or more small areas of cancer in the brain. It delivers highly focused beams of radiation to the affected areas while limiting exposure to the surrounding healthy brain tissue.

Immunotherapy

Immunotherapy drugs stimulate the immune system to kill cancer cells. They are used widely to treat other types of cancer, including smoking-related lung cancer. However, non-smoking lung cancers do not always respond well to immunotherapy drugs. The reason for this is an ongoing area of research.

"The whole oncology team has been amazing. My CNSs, medical and clinical oncologists have all worked together and have supported me every step of the way." - Gini, living with EGFR

YOUR TREATMENT OPTIONS



This short animation explores the range of treatments currently available for non-smoking lung cancer. It provides a helpful overview of the options your healthcare team may discuss with you, and how your test results can influence the treatment plan recommended.

To watch, visit **ruthstraussfoundation.com/NSLC-videos**

WHAT IF NO TARGETABLE MUTATION IS FOUND?

Sometimes, testing doesn't find a driver mutation. This can happen if:

- The test didn't work properly, for example, there wasn't enough of the tumour in the sample. In this case, your doctor may suggest another biopsy or test.
- The test worked, but no driver mutation was found. This still gives your doctor important information to help choose the best treatment, even if it isn't a targeted therapy.

If you find yourself in either of these situations, you should discuss next steps with your doctor.

DID YOU KNOW?

Even if no mutation is found, there are still treatments that can help. The results guide your medical team in planning the most appropriate care.

My notes

WHO WILL BE INVOLVED IN MY CARE?

A person with cancer is looked after by a multidisciplinary team (MDT). This is a group of healthcare professionals with expertise in cancer care. The members of a non-smoking lung cancer MDT are likely to include:

- Clinical nurse specialist (CNS) - a highly experienced nurse who provides support and advice about lung cancer and its treatment.
- Medical oncologist - a doctor who specialises in treating lung cancer with drugs, such as chemotherapy or immunotherapy.
- Clinical oncologist - a doctor who specialises in treating lung cancer with drugs and radiotherapy.
- Surgeon - a doctor who specialises in removing tumours.
- Physician - a doctor who organises tests and procedures to diagnose and treat cancer.
- Radiologist - a doctor who reviews and reports on scans and X-rays.
- Pathologist - a doctor who examines tissue samples (biopsies) to help decide on the best course of treatment.
- Haematologist - a doctor who examines blood samples to help decide on the best course of treatment.
- Research nurse - a nurse who specialises in helping people join clinical trials.
- Genetics specialist - a doctor with expertise in DNA, driver mutations and their role in lung cancer.

"Having a CNS to turn to makes such a difference - she explains things clearly, listens when I'm worried, and helps me feel I'm not facing this alone." - Gini, living with EGFR

DID YOU KNOW?

Your care team will take time to explain your options and answer questions. You do not have to make decisions alone.

INSIGHTS FROM GINI HARRISON, LIVING WITH NON-SMOKING LUNG CANCER

Gini Harrison is a Professor of Psychology, EGFR Positive UK (EGFR+ UK) Research Trustee, non-smoking lung cancer lead at the Ruth Strauss Foundation, and a mother of two. She was diagnosed with stage 4 non-smoking lung cancer and has since become a vocal advocate for patient-centred care.

“First of all, don’t panic! I know when you are first diagnosed with cancer it can feel like the end is near, that’s not necessarily the case anymore.

Thankfully, because of research there are more and more options all of the time. When I was first diagnosed with EGFR Exon 20 NSCLC (non-smoking lung cancer), there were no treatments available in the UK for my specific type of genetic mutation. There are now two and several more in the pipeline.

Take the time to get all of the information you can. Talk to your oncologist to find out what genetic mutation is driving your cancer, and investigate the various treatment options that are available for it. Immunotherapy and targeted therapies have made huge breakthroughs in lung cancer in the last decade.

In the last couple of months alone I have met several long-term survivors (one who was diagnosed 34 years ago!) - they have given me incredible hope. So search out the stories of hope, and hang onto them. If it can happen to them, it can happen to you!

When it comes to involving our children and telling them, we have been open and honest from the beginning. My son is still too young to understand what is happening, but my daughter was five at the time of my diagnosis, so we decided to be as honest as we could with her. As a psychologist, I believe that age-appropriate truth is the best way to go. Kids are pretty intuitive, so if you try and hide things from them, imaginations can run wild because they realise something big is going on.

The Ruth Strauss Foundation has this amazing Family Support Service available. I would encourage anyone with children to reach out and get support on how to talk to their children.”

For information about the Ruth Strauss Foundation Family Support Service, visit: **www.ruthstraussfoundation.com/support**

ABOUT THE RUTH STRAUSS FOUNDATION

The Ruth Strauss Foundation was established in memory of Ruth Strauss, a mother of two young boys who died from incurable non-smoking lung cancer at the age of 46.

Following her diagnosis in 2018, Ruth became aware of two urgent gaps: the lack of specialist emotional support for families facing a parent's incurable cancer, and the need for greater awareness and research into non-smoking lung cancer.

Today, the Foundation exists to:

- **Build resilience** - ensuring that every family facing a parent's incurable cancer receives professional emotional support to help manage anticipatory grief and the impact of diagnosis, so children can continue to thrive both now and in the future.
- **Empower research** - advocating for and investing in non-smoking lung cancer research and awareness, working with patient-led organisations, industry and healthcare professionals to improve patient outcomes.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