



# For those who have squamous cell carcinoma of the lung

Causes, symptoms, treatment and research

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# Squamous cell carcinoma of the lung

Lung cancer is one of the most common forms of cancer in the world, along with colon cancer (both sexes), prostate cancer (men) and breast cancer (women).

Lung cancer can affect anyone, but it is more common among smokers. It is more frequent among people over the age of 50, but it can occur at any age.



In Norway, more than 3500 people are affected by lung cancer yearly, which makes it the third most common form of cancer, and lung cancer accounts for about 10 per cent of all new cancer cases in Norway. New, targeted treatment in the last several years have enabled many people to live much longer with lung cancer than before.

Malignant tumours originating in the cells of the lung tissue are referred to as lung cancer. Lung cancer can develop in all parts of the lungs, but it most often appears in the lung's upper lobe.

## **Causes and risk factors**

- The risk of lung cancer increases with the number of cigarettes smoked and the number of years a person has smoked. Passive smoking is also a risk factor.
- Asbestos is another risk factor for the development of lung cancer.
- A smaller number of lung cancer cases are possibly due to exposure to radioactive radon gas in the bedrock.
- Other risk factors include air pollution, including diesel exhaust, as well as nickel and chromium exposure.
- New research, such as the study presented in 2022 at ESMO, Europe's largest congress for medical oncology, shows that air pollution can lead to lung cancer in people who have never smoked.

The risk of lung cancer is especially high for smokers who have also been exposed to asbestos or radon gas.

## Small cell and non-small cell lung cancer

Lung cancer is roughly divided into two types, small cell and non-small cell. Non-small cell lung cancer is the most frequent, accounting for around 85 per cent of cases. Small cell lung cancer is the most aggressive type of lung cancer as it often spreads quickly to other organs, and accounts for roughly 15 per cent of lung cancer cases.

Non-small cell cancer is divided into two main groups, based on the original cell where it arose:

- Squamous cell carcinoma: A tumour originating in the mucous membranes that line the inside of the respiratory tract. The tumour often grows in a central area in relation to the large bronchial branches. This is the second most common form of lung cancer.
- Adenocarcinoma: A tumour that originates in the glands that line the lung tissue. The tumour often grows further into the lung tissue. This is the most common type of lung cancer, and the type that is becoming more prevalent.

## Squamous cell carcinoma

About 25 percent of all patients with non-small cell lung cancer tumours have squamous cell carcinoma. Left untreated, squamous cell carcinoma is a serious form of cancer that tends to spread along lymph pathways to lymph nodes and other tissues and organs.

The epithelium, or epithelial tissue, is a cell layer that lines the inner and outer surface of the body, or that forms glands. In the lungs, the epithelial layer ensures the rapid transport of substances through the cell layers.

Currently, patients with squamous cell carcinoma do not undergo genetic testing, as no genetic mutations have been identified for therapy.

## Symptoms

The most common symptoms of lung cancer are coughing and shortness of breath, but these symptoms are also common in many other diseases. In lung cancer, the symptoms do not improve over time. It is therefore important to see a doctor if coughing and shortness of breath last longer than what is common for a respiratory infection. Possible symptoms of lung cancer:

- Cough, especially a persistent dry cough that suddenly changes
- Shortness of breath
- Bronchitis or a cold that does not improve, even with antibiotics
- Repeated respiratory infections
- Wheezing or feeling out of breath
- · Hoarseness and trouble swallowing
- Coughing up blood
- General weakness and fatigue
- Significant weight loss for no apparent reason
- Pain in the torso and upper part of the of the abdomen, headache, dizziness, chest pain, hoarseness and trouble swallowing may be signs of metastases (the spread of cancer cells). Spreading to the bones may result in pain and fractures. A referral for an x-ray would be necessary for such symptoms affecting the arms, legs or back. If the x-ray suggests lung cancer, the patient will be referred to a specialist.

## Assessment

If the patient is diagnosed with lung cancer, doctors will try to determine the stage of the disease. The stage indicates how advanced the disease is, whether it has spread, and how difficult it will be to treat. It is generally easier to cure lung cancer when the disease is detected early.

The assessment should lead to a choice of treatment based on the diagnosis of the type of lung cancer, the location of the tumour and its extent, as well as the patient's level of function.

Methods used to determine the diagnosis will vary depending on the case. The following diagnostic methods may be used:

- Medical history, including occupational and smoking history, and a clinical examination
- Heart and lung function tests
- Comorbidity (other diseases the patient has), such as COPD or cardiovascular diseases
- Blood tests
- Radiological examinations. These may include:
  - X-rays: A chest x-ray enables doctors to see the tumour determine exactly where it is located in the lung.
  - Ultrasound: With an ultrasound examination (sonography), doctors can determine where the tumour is located, its extent or whether it has encroached upon nearby lymph nodes.
  - CT scan: A CT scan can show areas of the lung that are hidden by other structures in the chest, or that are not visible on the X-ray. With the aid of a CT scan, doctors can get a very accurate picture of the size, location and spread of the tumour as well as possible spreading to other organs.
  - MRI scan: An MRI scan provides precise images of the lungs and surrounding area with the use of a powerful magnetic field.
  - PET scan: A PET scan produces images of tumours and metastases. Before the examination, the patient is given a weak radioactive glucose solution. During the examination, the patient is slowly led through a scanner where images are taken of their entire body. Cancer cells need a large supply of energy and have a high rate of metabolism, so the glucose collects in these cells. It is easier to see the affected tissue on these images through the glucose solution.

- Bronchoscopy: During a bronchoscopy, the doctor guides a bronchoscope, which is a flexible tube about the thickness of a pencil, through the patient's nose or mouth down through the trachea and into the bronchi and its branches. The aim of this examination is to take tissue samples or biopsies by "washing" (rinsing the lungs) or using a small brush.
- Fine-needle biopsy: In a fine-needle biopsy, the doctor takes cells from the lung using a long, thin needle that is pushed through the chest wall. This method is used to determine whether the tumour is benign or malignant, and if possible to identify the type of tumour.
- Mediastinoscopy: A mediastinoscopy is used to examine the space between the lungs – the mediastinum – and to take tissue samples. This procedure is done under general anaesthesia.
- EBUS: An endobronchial ultrasound examination (EBUS) combines a bronchoscopy and an ultrasound. The doctor inserts an ultrasound probe at the end of a bronchoscope tube, and then takes tissue samples.
- Sputum culture test: A sputum culture test involves an analysis of sputum or mucus coughed up from the lungs. This contains cells that have loosened from the mucous membranes of the bronchi or other parts of the lung. It may therefore by possible to find tumour cells in this.
- CT-guided biopsy: A needle is inserted into the chest wall to take tissue samples from the tumour in the pleura (lung membrane) just inside the chest wall. A CT machine is used to guide a targeted removal of a tissue sample.

## **Biomarker test:**

Tumour cells from patients with squamous cell carcinoma in the lungs are tested for the expression of the PD-L1 protein. The test is done by taking a small tissue sample (biopsy) of the tumour tissue. The tissue sample is examined in a laboratory that specialises in pathology.



## Checklist for consultations on diagnosis and treatment

Once you have undergone the first examinations and been diagnosed with lung cancer, it is a good idea to bring a checklist along to a consultation with your doctor. Make sure to have everything explained to you as precisely as possible so that you can better understand what it means and what to do.

We have collected a few tips for the checklist:

## Questions about the diagnosis:

- Is the diagnosis certain or are there still uncertainties?
- Where exactly is the tumour located?
- How large is the tumour?
- What is the stage of the disease?
- Has the tumour spread outside the lungs?
- Should I have more tests done to confirm the diagnosis?

#### **Questions about treatment:**

- What is my prognosis?
- Will I be undergoing additional examinations?
- What is the treatment plan?
- Should I be treated at a clinic or a hospital specialising in lung cancer?



## Treatment

There are several treatment options for patients who have squamous cell carcinoma, either with or without mutations.

You may be offered surgery, traditional cancer treatments such as radiotherapy and chemotherapy as well as drugs targeting your type of cancer. You should discuss the different options with your doctor. The type of treatment selected largely depends on the stage of the disease, as well as the age and general condition of the patient.

Patients with operable lung cancer are discussed at a multidisciplinary team meeting (MDT). Here the options for surgery or other therapies are assessed.

Surgery or radiotherapy can lead to a cure for non-small cell lung cancer in the early stages. Patients who cannot undergo surgery may be given the option of radiotherapy. Chemotherapy alone is not curative, but it can increase the possibility of a cure when provided together with surgery and/or radiotherapy.

## What is PD-L1?

PD-L1 stands for *Programmed cell death ligand 1*. A high PD-L1 expression on tumour cells can bind themselves to the Programmed cell death protein 1 in immune cells and prevent them from fighting and neutralising cancerous tumours. There are several drugs that block this binding and that are available for treating various types of cancer.

PD-L1 inhibitors are drugs that help the immune system fight cancer cells.

## Surgery

Surgery with a curative aim can be a treatment option in earlier stages of lung cancer. Surgical removal of tumour tissue in the lungs is done with the intent of curing the patient. Surgery for lung cancer is a good option if the tumour can be removed as completely as possible. This treatment option is only used if the tumour is still limited to one area. Other measures may be implemented before surgery.

## Radiotherapy

Radiotherapy is used to damage the DNA of the irradiated cells, thereby killing the cells. This can kill the tumour cells. For non-small cell lung cancer, radiotherapy can be offered after surgery, as curative treatment instead of surgery, or as part of combined chemotherapy and radiotherapy for disease with spreading to local tissues (in the lungs). This will an increase the probability of a cure.

In many cases, stereotactic radiotherapy is used. Stereotactic radiotherapy is a medical treatment that uses a very precise, targeted and high dose of radiation.

Patients with metastases may be offered palliative and life-prolonging treatment with radiotherapy in addition to drug therapy.

Brain metastases can be treated with surgery and stereotactic radiotherapy directed at a certain area or the entire brain.

Radiotherapy of bone metastases can provide effective pain relief.

## Drug therapy

Regardless of the targeted therapy you receive, you will have blood tests taken before and during your treatment to monitor blood cell levels, and to see if your liver and kidneys are functioning properly.

#### Chemotherapy

Chemotherapy drugs or cytostatics are drugs that kill cells or inhibit cell growth and cell division. Chemotherapy is used and recommended following surgery for early stages of non-small lung cancer either alone or together with radiotherapy.

For patients with advanced (stage IV) lung cancer and squamous cell carcinoma, chemotherapy is part of the standard treatment along with immunotherapy. This combination has been shown to be more effective than chemotherapy alone.

#### Immunotherapy

Immunotherapy is cancer treatment that utilises the body's own immune system to attack the cancer. By inhibiting PDL1 expressed in the cancer cells, the immune cells can identify the cancer cells as dangerous and neutralise them. Immunotherapy is part of the standard treatment, along with chemotherapy. If the cancer cells have a high level of PDL1 proteins, immunotherapy can be given alone.

If the cancer progresses while you are on this therapy, it may be better to try other drugs. This is known as moving from one line of therapy to another. The good news is that new drugs are continually being tested in clinical trials.



## **Clinical trials**

All potential new drugs must be carefully tested to see if they work as they should and can safely be used by humans. Testing is conducted in what are called "clinical trials".

Clinical trials may be a good option for patients who need treatment for progressive cancer, as it has been shown that participation itself in clinical trials may result in a better prognosis. Patients who participate in a clinical trial are always closely monitored through tests, hospital visits and other follow up. In a clinical drug trial, patients are usually divided into groups for comparison in order to ensure clear results. Neither you nor the doctor will know whether you are receiving the drug to be tested in the study or whether you have been randomly placed in the control group.

Your doctor may ask you if you wish to participate in a clinical trial. Participation costs nothing and is entirely voluntary.

If you are considering taking part in a clinical trial, you should find out as much as possible about the study before deciding whether to join:

- What are the researchers trying to learn?
- Are there potential side effects linked to the drug being researched?
- What do I have to do?
- Where do I have to meet up?
- What are my rights and duties as a participant?
- What is the alternative if I do not wish to participate?

You can find an overview of ongoing clinical trials at **www.clinicaltrials.gov** or you can search for or go to **www.helsenorge.no/kliniske-studier** where you will find a list of all clinical trials in Norway.

There are also several clinical trials for targeted therapy that may be relevant for patients with squamous cell carcinoma of the lungs.

## Lifestyle - tips and advice

General health advice such as eating healthy and getting enough sleep and exercise is important for everyone, also patients with lung cancer. We do not have any special dietary advice for lung cancer patients, but for many patients, it can be challenging to get enough nutrition while undergoing treatment. Advice from a dietician or personnel with experience with cancer patients and nutrition can be beneficial. Lung cancer patients are advised to stop smoking for many reasons. Smoking can reduce your appetite. Quitting smoking will make chemotherapy and radiotherapy more effective and it reduces the risk of developing other types of cancer in patients that have been cured of lung cancer. When it comes to exercise, patients should do what they feel up to doing. It is pointless to force yourself to do strenuous exercise during this tough treatment, but it is a good idea to engage in some movement and physical activity.

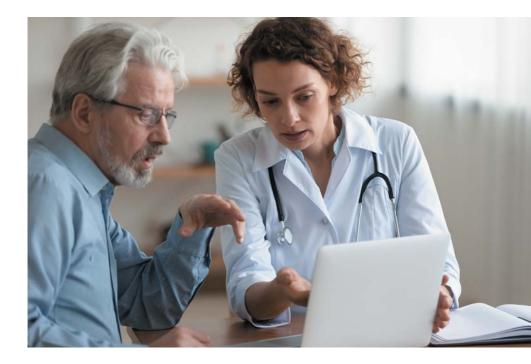
Additional tips on how to live with lung cancer can be found on the Norwegian Lung Cancer Society's website: www.lungekreftforeningen.no



## **Patient care pathway**

A standard patient care pathway describes how assessment, treatment, communication and dialogue with the patient, as well as the family members, distribution of responsibilities, and specific trajectory schedules are all organised. The purpose of a patient care pathway is to ensure that cancer patients receive a well-organised, comprehensive and predictable trajectory without unnecessary delays in assessment, diagnostics, treatment and rehabilitation. Among other things, a patient care pathway for lung cancer ensures that all hospitals treating lung cancer will have regular decision-making meetings with a multidisciplinary team (MDT) to ensure quality assurance of assessments and treatments. Participants in meetings for assessing lung surgery should include pulmonologists, thoracic surgeons, pathologists, nuclear medicine radiologists, and patient care pathway coordinators.

A patient care pathway has been designed for diagnostics, treatment and follow-up of lung cancer. See **www.helsedirektoratet.no** for more information on patient care pathways.



## **Current research**

## Improved screening

Treating non-small cell lung cancer in the earlier stages will give better results, which is why there is a strong interest in being able to detect lung cancer before symptoms appear. Researchers are investigating better screening techniques, such as genetic testing, to understand who may be at higher risk of developing lung cancer.

## Advances in radiotherapy and surgery

Work is being done to find ways to improve the effect of surgery and radiotherapy, while simultaneously reducing the side effects of these procedures.

## Liquid biopsy

In recent years, a great deal of research has been done on liquid biopsies. A liquid biopsy involves taking a blood test to identify DNA that has been shed from the patient's tumour cells. This may help find molecular changes that can be used to plan treatment, and it may replace or supplement a tissue biopsy. This may be useful at the time of diagnosis and perhaps even more so if the cancer progresses in order to ensure more targeted therapy. Research is also being conducted to learn whether lung cancer can be detected in blood samples at earlier stages of the disease.

## Drug therapy for lung cancer

There is a great deal of activity in the development of new drug therapies for cancer, and there are constantly new clinical trials. New drugs for targeted therapy are being tested, with accompanying advanced diagnostics. Some of these are very promising. Precision medicine for cancer treatment involves both diagnostics and treatment of very small patient groups. This requires collaboration between the clinical trials, with patients in many different countries.

There are also promising developments in immunotherapy. This involves the development of entirely new drugs and new combinations of established drugs. This is good news and more patients are expected to receive more effective treatment in the future. Patient story

"Have felt supported the entire way!"

"When lung cancer was suspected, it felt as though I was put on an express train! Everything went so incredibly fast, from the examination until I was in treatment.

For me, the patient care pathway for lung cancer worked extremely well. I am full of admiration for the healthcare personnel that have worked hard to help me feel secure and supported," says Ole Erik Melum (age 59) from Trondheim.

Ole Erik was actually convinced that his heart was the reason he had trouble breathing. In February 2021, he was sent by ambulance for the first time with suspected atrial fibrillation. In the weeks that followed, the ambulance was called to pick him up three weeks in row. He was put on blood pressure medication, and doctors found a slightly enlarged heart. But he still couldn't breathe, and in addition, he had developed a hypersensitivity to all types of smells.

#### From one diagnosis to another

"I visited my GP several times and was given asthma medication, among other things, but it didn't help. In December the same year, I was referred to a pulmonary specialist. Various breath tests were taken there, and the specialist believed that I probably had COPD. I was sent on for X-rays, where they found things, and then CT scan was quickly performed at St. Olavs. Shortly after the CT scans were done, a doctor at the department of pulmonology at the hospital called and wanted to admit me the following day. I was told that a stent was urgently needed. Everything was pretty confusing to deal with – from asthma to COPD to having to put a stent put in my chest."

When he was admitted, there was even more to deal with for Ole Erik and his husband Jonny. The doctors had changed their minds and wanted to assess him for cancer.

#### Good news

"Being told that I was going to be assessed for cancer was really the hardest thing for us. As the only survivor of three siblings, it was difficult to call my mother and tell her that the doctors suspected cancer!"

After many examinations, Ole Erik was told on 27 December that cancer had been confirmed. At the same time, there was also good news. He had a form of lung cancer that could be cured. The course of treatment was planned, and on 4 January 4 2022, he began the first of 33 radiotherapy treatments.

#### Good treatment outcome

It became apparent that the tumour was pinched around the main artery, so it was not surgically possible to remove it. However, the treatments he received were effective. The initial follow-up after radiotherapy showed that the tumour had shrunk by 40 percent. He was also given two rounds of chemotherapy, where each round was administered over a period of three days.

"After a while, I was also given immunotherapy through a research project. But in the second round, something happened to my metabolism and after some testing, the doctors decided I couldn't continue with it.

Fortunately, it turned out that Ole Erik benefited significantly from the treatments he had received. Because the tumour had shrunk, there was no longer any danger to his main artery and new checkups indicated that everything looked fine.

In late summer 2022, he was told there were virtually no active cancer cells left in his body.

#### Good help throughout

"It's an amazing feeling knowing I have responded so well to all the treatment. The follow-up I've received has been incredible throughout. I have been kept informed of all developments and what I can expect with respect to long-term side effects.

The radiotherapy was challenging because Ole Erik had to lie flat during radiation sessions, which made it more difficult for him to breathe. He was given help by building up with pillows as best as possible, and he was taught different breathing techniques that helped him manage all the radiotherapy treatments. During the treatments, he suffered radiation injuries to his neck and throat, but this has improved over time.

"It was mostly the discomfort, and not directly pain. If I talk too much my throat quickly feels dry, but it helps if I drink a lot of water."

#### No explanation for hypersensitivity to smell

What bothers Ole Erik the most is his shortness of breath, and that he is hypersensitive to all types of smells.

"My breathing may improve, I've been told, but the doctors can't give me an explanation for the problems with smells. It's so bad that it's hard to be around other people because all the smells become unbearable and overwhelming. I've worked in a store for 30 years and love my job, but I have now been on sick leave since the autumn of 2021. This is difficult for me, and it also affects my social life."

#### Good there are two of us

Ole Erik has felt an extra security of having his husband present at all examinations and important meetings.

"I'm so lucky to have a person who supports me so well. Having both of us there

to listen when receiving information from the doctors is incredibly important. We have also made a routine of writing down all questions in advance of meetings and checkups to make sure that we ask questions about everything we're wondering about. This has worked really well, and I highly recommend it."

Now in the autumn of 2022, Ole Erik is not on any type of cancer treatment, and he attends checkups every third month. So far, everything looks good.

"My focus is on being happy and trying to fill my days with good things. I'm not worried about the future. There are no guarantees of what's to come."



# Terminology

**ALK:** A gene that ensures the production of a protein in the body called ASL receptor tyrosine kinase.

**ALK mutation**: An ALK mutation (genetic alteration) occurs when the ALK gene is damaged and attaches itself to another gene.

**ALK inhibitors:** Anti-cancer drugs that act on and block (inhibit) the growth of cancer cells caused by ALK mutations.

**Biopsy**: A procedure that involves taking a tissue sample from the body in order to look for signs of disease. The tissue sample is examined for any changes or growth patterns.

**Brain metastases:** When the cancer has started in one place in the body, such as the lungs but spreads to the brain. This is still considered lung cancer, not brain cancer.

**Cancer**: A group of diseases caused by the uncontrolled division and growth of abnormal cells in parts of the body.

**Central nervous system:** Part of the nervous system that consists of the brain and spinal cord.

**EGFR**: A gene that ensures the production of a protein in the body called the epidermal growth factor receptor. A mutation of the EGFR gene may cause EGFR-positive lung cancer. **EGFR-inhibitors**: Anti-cancer drugs that act on and block (inhibit) the growth of cancer cells caused by EGFR mutation.

Fatigue: Another word for intense exhaustion.

**Gene**: Basic units made up of DNA sequences (genetic material) that determine such things as hair colour and eye colour.

Genetic mutation: An abnormal alteration of the DNA sequence in a gene. A somatic mutation is a mutation occurring in a gene that is not hereditary. These mutations are usually caused by environmental factors, but they can also occur spontaneously. A germline mutation occurs in cells that have developed into egg or sperm cells, which can then be passed on from parents to offspring. Gene mutations have various effects on our health depending on where they occur.

**Hereditary:** Something passed from parent to offspring through the genes. Characteristics or diseases children inherit from their parents.

**Line of treatment** (first-line, second-line, etc.):

First-line treatment is the first drug or treatment given to a patient for a specific disease (usually regarded as the best treatment for this disease). Second-line treatment can be given if the first drug is not effective enough for the patient. **Metastases**: When cancer spreads from one part of the body to another.

**Molecular testing**: A lab test that analyses certain changes in a gene or chromosome that could cause a certain disease or condition.

**Neuropathy**: Nerve damage that may be caused by drugs, tumours or surgery. Symptoms vary depending on which nerves have been affected. You may experience pain, extreme sensitivity, numbness or weakness. Symptoms are often most noticeable in the hands, feet or lower part of the legs. The nerves that control digestion and blood pressure may also be affected, which can lead to constipation, dizziness or other symptoms.

**NSCLC**: Non-small cell cancer. Approx. 85% of all lung cancer cases are NSCLC. ALK-positive lung cancer is one form of NSCLC and comprises approx. 4% of all NSCLC cases.

**ROS1**: ROS1 is a receptor tyrosine kinase (codes for the ROS1 gene), with structural similarities to the anaplastic lymphoma kinase (ALK) protein.

**Somatic (mutation)**: Non-hereditary genetic mutations that occur after birth, during a lifetime.

**Targeted therapy**: A type of cancer treatment that targets specific genes and proteins and disrupts the way specific cancer cells send signals or interact with each other. This can stop cancer cells from dividing and growing.

**Tumour**: A mass or lump caused by abnormal tissue growth. These can be benign (not harmful) or malignant (cancer).

#### Tyrosine kinase inhibitors (TKI):

Drugs that block chemical messengers (enzymes) called tyrosine kinase. Tyrosine kinase helps to send signals to cells that trigger growth. The inhibitors block the signals, which stops cells from dividing and growing.

## Norwegian Lung Cancer Society

The Norwegian Lung Cancer Society is a patient organisation for those who have or have had lung cancer, and for family members of lung cancer patients.

We provide advice and support, and we protect the interests of lung cancer patients. Together, we work to improve treatment and rehabilitation for lung cancer patients. We work to spread knowledge of lung cancer prevention, and to promote the issue of lung cancer before health authorities and politicians.

The Norwegian Lung Cancer Society has 800 members. We have local organisations, contacts in the county and peer support persons throughout the country. More detailed information about us and our peer support services can be found on our website.

Join our community – become a member of the Norwegian Lung Cancer Society: www.lungekreftforeningen.no

#### Contact us:

E-mail Secretariat: post@lungekreftforeningen.no Phone Secretariat: 93470121 – the phone line is open Monday through Friday, 09:00– 15:00

#### Peer support services:

Living with a serious illness involves experiences that can make us feel alone. Family members may also feel alone with the uncertainties and concerns this entails. The Norwegian Lung Cancer Society therefore aims to provide a community for people in the same situation. We have peer support persons who are patients and family members who have gone through the process of the disease and have been trained to provide support to others who have found themselves in the same situation.

You can contact the Norwegian Lung Cancer Society's peer support persons directly. See the list of our peer support persons on our website: www.lungekreftforeningen.no/likepersontjenesten You can also send an e-mail to likeperson@lungekreftforeningen.no



Community Unity Security

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Phone 93470121 post@lungekreftforeningen.no **lungekreftforeningen.no**