



For those who have Small cell lung cancer

Causes, symptoms, treatment and research

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Small cell lung cancer

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 3,000 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.

Malignant tumours originating in the cells of the lung tissue are referred to as lung cancer. Lung cancer may 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 considered a 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.

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 common and accounts 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, accounting for roughly 15 per cent of lung cancer cases.

Symptoms

The most common symptoms of lung cancer are coughing and shortness of breath, but these symptoms are also common for 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 knees and upper part of the abdomen, headache, dizziness, chest pain, hoarseness and trouble swallowing may be signs of metastases (the spreading 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.

Small cell lung cancer

About 450 people are diagnosed with small cell lung cancer in Norway each year. This type of lung cancer is often aggressive, grows quickly and spreads early. This is because the cancer cells divide rapidly. That is why symptoms may appear suddenly, sometimes within a period of a few weeks. If the tumour is located in the central area of the respiratory tract, it can narrow the airways and cause shortness of breath. A few tumours may grow and begin squeezing important blood vessels to the lungs and within the space between the lungs. This space has the Latin name “mediastinum”. This may cause

symptoms such as facial swelling and distended blood vessels on the neck. If the tumour has spread to other organs, symptoms may come from them. If the tumour spreads to the brain, it can cause symptoms resembling a stroke. In small cell lung cancer, some tumours may secrete hormone-like substances. One of these substances causes the body to excrete too much salt so that the level of sodium in the blood decreases and is too low. This may lead to nausea, vomiting, confusion or cramps.

Small cell lung cancer is roughly divided into two stages – limited and extensive. The difference between them is that a limited stage cancer can pass through what oncologists call a radiation field. Around 35 per cent, or roughly 150 patients with small cell lung cancer have a limited stage disease. These patients are treated with the aim of curing the disease and making them healthy again. The remaining 300 patients who are diagnosed with extensive-stage small cell lung cancer cannot be cured, but therapy will often reduce their symptoms significantly, extend their lives and improve their quality of life.

Assessment

The purpose of the assessment is to determine which disease the patient has, if the cancer has spread to lymph nodes or other organs, and how the patient will tolerate the examinations and therapy. Comorbid diseases, the use of medication and how the patient functions in daily life are all carefully assessed. Breath tests are conducted to examine the patient's lung function. Blood tests are performed to check for liver and kidney function.

Some patients are referred for assessment based on a lung x-ray. However, it is not always possible to detect lung cancer on an ordinary x-ray. This is why all patients with suspected lung cancer must have a CT scan (computer tomography) of their lungs and upper part of the abdomen, preferably with a contrast medium. The CT scan shows where the tumour is located and can determine whether it has spread. Based on the CT scan, doctors will decide whether to take a tissue sample for biopsy. Tissue biopsies are essential for providing the correct therapy. There are several ways to get a tissue sample for biopsy:

- **Bronchoscopy** The patient is usually awake but is given an intravenous sedative, and a local anaesthetic is administered to the throat and airways. The pulmonologist will either direct the scope through the patient's mouth or nose to check the appearance of the respiratory tract, and they will take tissue samples of visible changes. Sometimes a tissue sample will be taken while using an x-ray if the tumour is not visible from the inside. It is also possible to use an endobronchial ultrasound (EBUS) to look for changes in the tumour or lymph nodes located under normal tissue, and then do a fine-needle biopsy of this. The examination is not painful, but most patients will cough and experience a little discomfort until the anaesthetic takes effect. After the examination, the patient may cough up some blood, and a few may develop a fever later in the

evening. It is important to fast for four hours prior to the examination, and you will be instructed what to do if you are using blood thinner medication.

- **Ultrasound-guided biopsy** Tumours located near the chest wall can be viewed with an ultrasound, and the radiologist or pulmonologist can then take biopsies of these with the aid of the ultrasound. It is also possible to take a sample of the fluid around the lung or pleura with this method. During this examination, the patient is awake and is given a local anaesthetic. An ultrasound can also be used to take samples of tumours in other organs, such as the liver or bones to determine the spread of the lung cancer or other types of cancer.
- **CT-guided biopsy** If the tumour is located in an area that is not possible to see from the inside with a bronchoscope or from the outside with an ultrasound device, a CT-guided biopsy may be performed. This enables biopsies of smaller tumours located in healthy lung tissue. The patient is given a local anaesthetic, and a specially trained radiologist takes a sample of the tumour while simultaneously watching the CT scan where the needle is located in order to target the tumour. Some patients may have a punctured lung after this examination, but this will heal in most cases without doing anything other than checking to make sure that the lung re-inflates. A CT-guided biopsy of other organs may also be performed if metastases are suspected.

The tissue samples are carefully examined by a pathologist. Both the appearance and features of the samples are described and dyed to determine the origin of each tumour tissue. This is important for examining whether it really is lung cancer, whether the cancer has spread from another place in the body, or if it is an inflammatory disease resembling cancer. Currently, genetic analyses are not standard procedure in the assessment of small cell lung cancer. This is because we unfortunately cannot offer tailored therapy based on genetic analyses of people with small cell lung cancer. However, research is being done in this area, and it is possible that genetic analyses of small cell lung cancer will become part of such assessments.

The spread of a tumour can be seen on a CT scan, but a PET-CT is also used to identify spreading to other parts of the body. PET-CT scanning should be performed on all patients where the disease appears to be limited. In patients where spreading to several areas can be seen on a CT, a PET-CT would be unnecessary. PET-CT scanning is an examination where the patient is given an intravenous injection of a small amount of radioactive glucose. This glucose is absorbed in areas with high metabolic activity, such as cancer cells. In the brain, the rate of glucose absorption is so high that it is not possible to see any tumours. This is why an MRI of the brain is necessary to determine spreading. This should be done on all patients with limited stage small cell lung cancer. Patients that have metal or medical instruments in their bodies (e.g. pacemakers not approved for MRI machines) cannot undergo an MRI and must instead have a CT scan of the head.

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 you can 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 my treatment plan?
- Should I be treated at a clinic or a hospital specialising in lung cancer?



Treatment of small cell lung cancer – limited stage

When the spread of the disease fits within a radiation field, this is referred to as a limited stage. The aim of this therapy is to cure the patient. In very few cases, the cancer is discovered so early that there is healthy lung tissue on all sides and it has not grown into central chest structures. In this case, it would be possible to surgically remove the cancer along with the lobe of the lung it is located in. However, this happens very rarely with small cell lung cancer, with only a few such cases per year in Norway. Most patient with limited stage small cell lung cancer are treated with a combination of chemotherapy¹ and radiotherapy. This is a tough therapy, and basically a full-time job over a period of about 12 weeks.

Chemotherapy is administered as a combination of two substances, etoposide and a platinum-based substance (carboplatin or cisplatin), which are administered intravenously. On the first day, both substances are administered, and on days 2 and 3, the patient is given another dose of etoposide. After another three weeks, on day 22, the patient is given another round. There will be a total of four such rounds.

Earlier, patients were given radiotherapy directed at the chest twice daily for 15 days, but a Norwegian research study (the THORA study) has shown that life expectancy is increased by administering radiotherapy for 20 days. Radiotherapy is performed twice daily for 4 weeks, meaning every weekday with a break during weekends, for a total of 20 days. Radiotherapy will begin after chemotherapy has been initiated.



¹ Chemotherapy is a cytostatic drug therapy using chemicals to destroy cells. In this brochure, we have chosen simply to use “chemotherapy”.

Treatment of small cell lung cancer – extensive stage

From 1 November 2021, the standard treatment in Norway for extensive stage small cell is immunochemotherapy, which is a combination of two types of chemotherapy (carboplatin and etoposide) together with atezolizumab. Four rounds of this mixture are given intravenously every three weeks, and then immunotherapy (atezolizumab) is administered every four weeks as maintenance therapy. Not all patients are able to tolerate all three drugs, so it may be necessary to make adjustments to the therapy.

Two international studies have shown that immunotherapy given together with chemotherapy results in a somewhat higher survival rate (Horn et al. NEJM 2018; Paz-Arez et al., Lancet 2019) as opposed to only administering chemotherapy. Immunotherapy is then given alone as maintenance therapy as long as the patient benefits from this, or until unmanageable side effects arise.

Radiotherapy may be relevant for specific symptoms. For example, if the cancer spreads to the point where it presses on the airways or blood vessels in the chest, or to relieve pain due to metastases to the bones.

Prophylactic whole-brain radiation

After completing treatment, both in the case of limited and extensive stage cancer, a CT scan of the chest will be performed to determine the effect of the therapy. Most patients experience a good effect of the therapy, and they are then offered prophylactic whole-brain radiation. This is done to prevent a recurrence and spreading of the disease to the brain. This has been shown to increase life expectancy. Radiation to the brain also has some side effects. Nausea, fatigue and headache may occur, and some patients experience memory loss. Radiotherapy is often given over a period of 2 weeks with a total of 10 treatments. Whole-brain radiation also damages the hair follicles, but the hair will grow out again afterwards. An alternative to whole-brain radiation is to follow up with MRI control scans of the head every third month.

Treatment if the cancer returns

Many patients with small cell lung cancer experience a recurrence. A new round of chemotherapy may then be relevant if the patient is physically able to withstand it. Depending on how much time has passed since the previous treatment, a new round may be administered. If a long time has passed since the first round of therapy, it may be possible to try the same combination again, although there are other drugs and combinations of chemotherapy that can provide relief and control the disease.

Treatment side effects

Chemotherapy

Chemotherapy affects cells that divide at a high rate – not only the tumour but also other healthy cells in the body that are frequently dividing. These are cells in the gastrointestinal system and cells in the bone marrow, which form blood cells. Therefore, side effects will often appear in the gastrointestinal system, or as a result of a temporary weakening of the bone marrow.

Nausea is common, but this can be prevented and treated with anti-nausea medication. Many develop constipation and must use medications to ease bowel movements. Some patients experience diarrhoea. When chemotherapy is given together with radiotherapy, the cells in the oesophagus often become damaged. This can cause soreness of the oesophagus and difficulties with eating. Analgesics and changes to the diet can ease some of the problems, but some patients must have temporary tube feeding due to the side effects. Some patients may also develop a fungal infection of the mouth and oesophagus, which can make it difficult to eat. This can be treated with a mixture or tablets.

When bone marrow is temporarily knocked out by chemotherapy, this affects the formation of red blood cells (haemoglobin), white blood cells (which form the most important part of our immune system) and platelets (which prevent bleeding). This can result in anaemia, which is a low red blood cell count that can result in fatigue, as well as a higher risk of infection (bacterial and viral infections), and bleeding. The immune system is at its weakest 7 to 14 days after chemotherapy, and it is common in many places to do a blood test around this time to check how you are doing. It is crucial that you contact your doctor if you develop a fever or symptoms of infection during the period where your immune system is weak. Some patients will require hospitalisation and treatment with antibiotics. When your immune system is weak, your body may not react to an infection in the same way as before. There may be less snot when you get a cold or less coughing with pneumonia. You may just feel very tired, in poor health, or just lose your appetite. It is essential that the patient and treating physician agree on who should be contacted if the patient develops symptoms that may indicate an infection when the immune system is weak. At many hospitals, patients are given a direct number to the department that they can call when such problems arise.

Fatigue and tiredness are common during chemotherapy. Etoposide will cause hair loss, and patients will then be entitled to financial support for a wig. Cisplatin can cause nerve damage or polyneuropathy. This may result in changes in sensation in your fingers or feet. You may, for instance, feel that you are walking on pillows. Some experience a tingling or prickling sensation in their fingers or toes. Changes in taste may also occur. Cisplatin may cause hearing loss and should not be given to patients who already have poor hearing. Chemotherapy may also affect kidney function, especially cisplatin.

The principle behind immunotherapy is entirely different than chemotherapy, and the side effects also differ. There may be side effects from nearly all of the organs, and they may be severe. Immunotherapy involves antibodies that attach themselves to cancer cells or immune cells so that the disease becomes more visible to the immune system. Our immune systems are trained to recognise bacteria, viruses and other foreign substances in the body. This triggers reactions to surround or destroy foreign substances or render them harmless. However, cancer cells have ways of making themselves invisible to the immune system, or to inhibit the immune system's attempts to destroy the cancer. Immunotherapy is designed to block the ability of cancer cells to make themselves invisible to the immune system. To put it another way, the brakes of the immune system are suppressed – and the gas pedal is pushed instead. When the immune system's gas pedal is pushed, it may misunderstand and attack healthy cells in the body and not just cancer cells. This is why immunotherapy may result in inflammation (without bacteria) in nearly all of the body's organs, such as the lungs, kidney, liver, pancreas, thyroid gland and intestines. Patients with autoimmune diseases or diseases that require the use of immunosuppressants cannot be given immunotherapy.

Immunotherapy must be carefully monitored with blood tests to assess metabolism and liver and kidney function, and the patient's symptoms must also be observed. Side



effects that impact organ function are not frequently seen, but they must be recognised and taken seriously. Sometimes side effects are treated with drugs and pauses in immunotherapy, while other times the therapy must be permanently discontinued. The most common side effects of immunotherapy are fatigue and skin itching.

As with side effects of chemotherapy, it is important that the patient knows where to turn if something happens, and that side effects are reported to healthcare personnel who are familiar with these.

Checkups

Once the treatment has been completed, patients are checked with a CT scan of their lungs. Patients with limited stage cancer have checkups with 3-6 month intervals, while patients with extensive stage cancer will usually have CT scans more often if it may be necessary to start chemotherapy again. It is also important for patients to contact their doctors in between checkups to let them know about any symptoms or signs that may indicate a recurrence of the disease, so that the checkup can be rescheduled at an earlier date. If things are going well and there are no signs that the disease has returned after 2 years, the intervals between checkups can be prolonged. It is common to follow up lung cancer patients until five years after they have finished treatment. At that point, it is possible to declare them cured of their cancer.

Long-term side effects of treatment

Radiotherapy of the lung tissue can result in a lung inflammation known as pneumonitis. The lung inflammation is not caused by bacteria, but the symptoms are similar. This is a reaction in the lung tissue to radiation, and it usually occurs one to three months after radiotherapy is finished, but it can also occur later. Symptoms include shortness of breath and a dry cough. Fever may also occur. It is important to let your physician know about these symptoms, as they can be treated. Some patients will, however, develop permanent damage to their lung tissue following radiotherapy. This may result in coughing and shortness of breath that does not entirely disappear. Side effects such as hearing loss and polyneuropathy may be persistent and can become chronic. Kidney failure due to chemotherapy often improves, but not always. Fatigue may remain long after the treatment is over. Some patients also develop symptoms of anxiety and depression after experiencing a serious illness and tough treatment.

Lifestyle – tips and advice

General health advice such as eating healthy and getting enough sleep and exercise is important for everyone, also patients with small cell 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.lungekrefeforeningen.no

Patient care pathway

A standard patient care pathway describes how assessment, treatment, communication and dialogue with the patient and family members, distribution of responsibilities, and specific trajectory schedules are all organised. The aim of a standard patient care pathway is for cancer patients to 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 therapies. 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

Norwegian research and ongoing studies:

The Norwegian ACHILES study examines whether offering immune checkpoint inhibitors following standard chemotherapy and radiotherapy increases life expectancy for patients with limited stage, small cell lung cancer. The cancer research environment at NTNU in Trondheim is also planning a study to examine the effects of immune checkpoint inhibitors in patients with extensive stage small cell lung cancer, in addition to standard chemotherapy and thoracic radiotherapy. There is also hope that genetic mapping of cancer can provide new points of attack for targeted therapies, as in the Norwegian IMPRESS study. Perhaps this will also enable researchers to discover new ways of treating small cell lung cancer.

An overview of clinical trials in progress in Norway can be found at HelseNorge www.helsenorge.no/kliniske-studier

A Norwegian site called MED.hjelper is intended to help patients to find Norwegian clinical trials: www.medhjelper.com/finn-kliniske-studier

International research:

Internationally, studies are examining combinations of several immunotherapy drugs in addition to chemotherapy for extensive stage cancer. There are also therapies under consideration by pharmaceutical authorities for the treatment of relapsing extensive stage cancer. For an overview of international clinical trials, see:

www.clinicaltrials.gov

www.clinicaltrialsregister.eu

Patient story

Completed the Vasaloppet ski race after lung cancer treatment





Ole Knutzen (age 67) was in good physical condition and looked forward to competing in the Vasaloppet ski race for the eighth time when in late 2012 he began noticing shortness of breath when he was out training. Shortness of breath and later coughing was eventually diagnosed as small cell lung cancer.

“I’m grateful that my GP understood the severity of my symptoms and sent me for an x-ray the day after my doctor’s appointment. I believe he saved my life that day by pushing the right buttons in time!

Increasingly poor physical condition

In the weeks before Ole visited his GP, he noticed that his physical condition was gradually becoming worse. After he had stopped smoking and started exercising at age 48, he completed many cross-country ski races and got into shape. He consulted a doctor for the first time in early 2013, but the locum physician he saw believed that his symptoms at the time could be due to his suspected mononucleosis. He accepted this explanation, even though he had to give up already at the starting line during the Vasaloppet ski race in March. By Easter time, he was so unwell that he had trouble pushing his grandchild in a pram. He then understood that he had to return to the doctor. His GP did some quick examinations and sent Ole for an x-ray the following day. The x-ray led the doctors to perform an immediate CT scan, and that same morning, the GP phoned and asked Ole to come in for a talk. He was told that the radiologist had found a tumour.

A bronchoscopy confirmed the find. Ole was told he had limited stage small cell lung cancer, with a tumour that was 6.5 x 6.8 cm in size.

Completed treatment in August 2013

“Once I was diagnosed, everything happened quickly. I have undergone four rounds of chemotherapy and radiotherapy to the tumour 15 times. After that, I was given prophylactic whole-brain radiotherapy 15 times. In August 2013, the treatment was completed. I tried not to Google, and I wasn't sure how serious it was. I entered into a bubble where I just focused on looking ahead and that this was something I would be able to get through.

During his treatment, Ole experienced nausea due to the chemotherapy, and the radiotherapy led to pain upon swallowing. He also felt weak. The brain radiation resulted in further nausea and vomiting.

Long-term effects

Just over six months after treatment ended, Ole was back at work full time, and he had started fitness training.

“In March 2015, I completed the Vasaloppet for the eight time. It took me nearly twelve hours, but this was without a doubt the race I am most proud of having completed!

Ole continued working until the autumn of 2016 when the long-term side effects began taking a toll on him. He therefore took early retirement.

“The fatigue made me weak, tired and exhausted, something I struggle with daily. I also have radiation damage to my oesophagus, which is bothersome. In my experience, there is a huge potential for improvement by informing patients of the long-term effects that linger long after the treatment is completed. In the last few years, I find that if I exert myself a little too much, I start gasping for breath. By chance, an oncologist mentioned the importance of checking my heart after completing lung cancer treatment. In 2020, I had my heart examined, and a small leak in the valve on the left side of my heart was detected. For the moment, this isn't dangerous, but it could develop. I will be called in for a new checkup in three years. Many people don't know that radiation near the heart can lead to complications.

No relapse

“In 2018, after 64 treatments and five years of checkups, I was told that my treatment was completed. I have had no recurrence and am not taking any medication. Perhaps the reason it has gone so well for me is that I was in good physical shape before I got cancer, and that I've tried to stay active between treatments as well, despite having many difficult days.”

Today Ole lives a good life with his family. He does peer support work and is on the Board of the Norwegian Lung Cancer Society. He also makes time for a little fitness training.

“Even though I've adapted, it doesn't mean that I have accepted the disease. The fear of a relapse is always present, but I have learned to live with the fear and not let it control my life.

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 at www.lungekreftforeningen.no

Contact us:

E-post Sekretariat: post@lungekreftforeningen.no

Phone Sekretariat: **93470121** – the phone line is open Monday through Friday, from 09:00 to 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, as well as family members who have gone through the process of the disease, and who 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

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