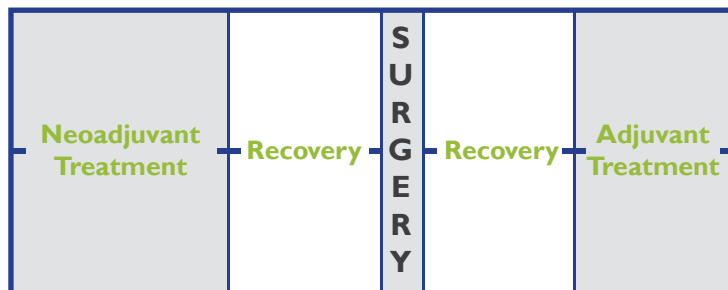


Neoadjuvant and Adjuvant Treatments for Non-Small Cell Lung Cancer



Neoadjuvant and adjuvant treatments refer to additional cancer treatments *before* surgery (*neoadjuvant*) or *after* surgery (*adjuvant*) offered to someone for their non-small cell lung cancer (NSCLC) where the surgery is carried out with the intent to cure the disease.

The purpose of these treatments is to reduce the chance of cancer coming back after it is removed by the surgery and to improve overall life expectancy.



Having an operation depends on doctors being confident that they can remove all the cancer cells.

Doctors consider many factors in deciding if surgery with neoadjuvant or adjuvant treatment is possible for you, particularly identifying the location, size and spread of your lung cancer. This is known as *staging*.

Doctors stage a person's cancer using numbers 1 to 4, giving stage 1, stage 2 and so on, where stage 4 refers to the most advanced and widespread cancer. Surgery is generally only considered when the cancer is still in one place (within the lung) and has not affected any parts of the body beyond nearby lymph nodes.

Stages of NSCLC can be subdivided and the stages that may be considered for surgery include stage 1A, 1B, 2A, 2B or 3A. Staging is complex and your doctor will explain how it applies to you. The type and stage of your lung cancer are also important in deciding if neoadjuvant or adjuvant treatments may be options for you.

This may be because the tumour is in a position that is too difficult or dangerous to operate on or because the person has other health issues that make them unfit for major surgery.

If surgery removes all the cancer, why are neoadjuvant and adjuvant treatments necessary?

Over time, cancer cells can break away from the original tumour as it grows and spreads throughout the body. It can be very difficult to know if and when this happens.

This means that, although the primary cancer may be removed, stray lung cancer cells (*micrometastases*) may already be circulating in the body outside the lung and so would still be there after lung surgery.

To help prevent this happening, neoadjuvant and adjuvant treatments aim to reduce the cancer cells that have broken away from the primary tumour to a minimum, if not completely, to prevent or delay cancer coming back.

What types of treatments are used?

In addition to surgery, depending on whether you are having neoadjuvant or adjuvant treatment, other treatments may include:

- chemotherapy – kills fast-dividing cells (cancer cells)
- immunotherapy – supports the body's immune system to recognise and kill cancer cells
- targeted therapy – kills and slows down the growth of cancer cells that have genetic changes (mutations)
- radiotherapy – uses high energy X-rays (radiation) to destroy cancer cells while avoiding normal cells.

Chemotherapy and immunotherapy are typically given by intravenous injection (IV) roughly every three weeks, and targeted therapies are daily tablets.

Many people experience side effects from these treatments. Side effects can be wide ranging from mild to severe. Your medical team will speak to you about side effects that may be caused by your treatment. You can then weigh up any harms against possible overall benefits you may experience.

These treatments do reduce the risk of your lung cancer coming back but, despite treatment (and associated side effects), your cancer may still come back.

How these treatments are used, singly or in combination, varies from country to country. This is a quickly advancing area of cancer medicine so some may be available to you as standard practice and others as part of a clinical trial. Others may not be available to you at all.

Your doctors will always recommend the best options for you given the type and extent of your cancer, your general fitness and any other health conditions. The fitter and healthier you are, the better you are likely to tolerate and respond to the treatment. You always make the final decision about going ahead with any treatment.

Before surgery, you will be encouraged to be more active, eat as well as you can, drink less alcohol and stop smoking. This approach is known as prehabilitation and these lifestyle changes can improve your outcomes from surgery and other treatments.

Neoadjuvant treatment

Neoadjuvant treatment is a treatment that is given to some people with operable non-small cell lung cancer (NSCLC) before their surgery to improve their overall outcomes.

Recent studies have shown that adding immunotherapy to chemotherapy neoadjuvantly can improve outcomes. You would likely receive three cycles of treatment (a cycle is a treatment plus a three-week recovery period).

It appears that by giving these treatments while the tumour is still present may increase and extend the body's immune system response to cancer cells.

This can more effectively reduce both the cancer in the lungs and any micrometastases circulating elsewhere.

Neoadjuvant treatment can also affect the type of surgery you may have. It can mean that operations are smaller, shorter and less invasive.

After your last treatment, you may have a recovery period of up to nine weeks before your surgery depending on the type of treatments you have had and how well you have tolerated them.

Your cancer doctors would carefully monitor your progress after each cycle of treatment and this will be checked on a scan, in consultation with your surgeon, before your operation is confirmed.

Benefits of neoadjuvant treatment may include:

- systemic treatments received earlier when a person is in better health to tolerate treatments (they are likely to be fitter and stronger)
- early treatment of micrometastases
- possible cancer downstaging before surgery with curative intent
- shorter, less extensive surgery, including more VATS and RATS operations

On the other hand, early systemic treatment introduces a longer time before surgery and this may cause anxiety in those waiting. In a small number of people, their cancer may grow bigger despite having neoadjuvant treatment and this can complicate surgery or even, in some circumstances, mean that surgery is no longer possible.

Immunotherapy may cause tumours to appear larger following treatment due to *pseudo-progression*, or *tumour flare*, making some decisions about continuing to surgery more difficult.

Adjuvant treatment

Adjuvant treatment is a treatment that is given after surgery. Doctors can tell from tests on tissue removed during surgery (*pathology*) if all the cancer cells have been removed around the site of your tumour (often called *clear margins*). However, they are less able to know for sure that there are no cancer cells circulating around your body that

Chemotherapy has been used as adjuvant treatment for many years as it has been shown to give small but significant increase in the chances of curing lung cancer after lung surgery if no further treatment is given.

Immunotherapy has not been shown to make significant improvements on its own but, for a certain group of patients, when given after chemotherapy, it gives further improved outcomes following surgery.

If your NSCLC has been found to have a particular genetic change (mutation) then you may be offered a targeted therapy as this has been found to improve outcomes.

After surgery for small, early-stage lung cancer there is less risk of lung cancer coming back so systemic treatments may not be considered as readily as if it were larger or had spread to nearby lymph nodes, for example. Your doctors will talk through these possible harms and benefits so that you can make your own decision.

Radiotherapy may be used on its own or in combination with chemotherapy in some cases, particularly if some cancer cells are found to remain at the site of the surgery.

You will have some recovery time, at least a month but up to three months, after your surgery before starting adjuvant treatment.

Benefits of adjuvant treatment may include:

- shorter time before surgery, compared to neoadjuvant treatment, reducing chance of your cancer spreading
- decision to operate based on scan immediately before surgery
- longer treatment (without a surgery deadline) which may allow for better control of the cancer.

On the other hand, some people may not tolerate adjuvant treatment well so they may have a better quality of life without it.

Is it possible to have treatment before and after surgery?

Most people who have neoadjuvant chemotherapy and immunotherapy do not have any adjuvant treatment. There are studies where people with operable NSCLC have had neoadjuvant chemotherapy and immunotherapy followed by adjuvant immunotherapy where outcomes have improved. These treatments may be referred to as *perioperative* treatments.

Clinical trials are ongoing and it is not yet clear if the perioperative approach is any better than neoadjuvant treatment on its own or adjuvant treatment on its own. Advances are being made all the time in this area so ask your cancer doctor if this is a treatment option for you.

Looking ahead

These are exciting times for lung cancer treatment. Lung cancer screening is increasing the number of people whose lung cancer is found at earlier stages. Along with advances in neoadjuvant and adjuvant treatments, curative treatment that includes surgery is an option for more people.

Researchers are continually working to identify microscopic elements of cancer and other cells that could radically improve matching the most effective treatments to a person's unique lung cancer characteristics

Artificial intelligence (*radiomics*) is also being used to potentially uncover tumoral patterns and characteristics that are difficult to identify or quantify by simply looking at scans.

These will improve how doctors can help maximise cancer management and therefore improve people's longer-term outcomes.



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This information leaflet has been produced by the Global Lung Cancer Coalition (GLCC) secretariat and reviewed by lung cancer experts. For more information on the support and information services available in your country, visit www.lungcancercoalition.org Version 1 – November 2024.