Targeted therapies for lung cancer
Introduction

If you or someone you care for has lung cancer, and targeted therapy is a possible treatment, then it’s almost certain that you will have a lot of questions.

We have produced this booklet in partnership with lung cancer experts and people affected by lung cancer to help you make positive, informed choices about your care and treatment. Use this booklet along with the information provided by your healthcare team.

Remember that most healthcare professionals are only too happy to answer your questions and help you with things that may be unclear or causing you concern.

We hope that this booklet answers your questions about targeted therapies. If you would still like to talk to someone about this, call our free and confidential Ask the nurse service on: 0800 358 7200 or email: lungcancerhelp@roycastle.org

You can also contact one of the many support organisations available in our Living with lung cancer booklet. Order a copy by calling us on 0333 323 7200 option 2, or look on our website: www.roycastle.org/usefulcontacts
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Understanding targeted therapies for lung cancer

What is a targeted therapy?
Cancer grows and spreads by cells dividing. This is controlled by chemical processes within the cell which send a signal to start the cancer cells growing. Sometimes a drug can be designed that blocks this chemistry. This is called a targeted therapy. Targeted therapies are also sometimes called biological therapies.

There are various types of targeted therapies used to treat lung cancer. Each works in a different way, and as researchers learn more and more about how cancer cells change and spread, newer targeted therapy drugs are being developed that focus on these changes to stop the growth and spread of cancer.

Targeted therapies aren’t a cure for lung cancer. However, they may stop the growth of your cancer and sometimes even shrink the tumour and lengthen your life. They may also help improve your quality of life, for example, by reducing coughing, making your breathing easier and helping to reduce pain.

“My consultant said we’re going to put you on a targeted therapy.

I’ve started taking one tablet every day, and I’d say eight weeks after that began, I was able to go shopping and meet people and say I feel a lot better now.

Liz
How do doctors decide if targeted therapy is right for me?
Targeted therapies only work for some people with non-small cell lung cancer (NSCLC). To find out if a targeted therapy may be suitable for you, cancer doctors will have to test some of your cancer cells (a biopsy).

The doctors are looking for specific characteristics that are different in some NSCLC cancer cells, and show up in the genes within the cells.

These are called mutations, and the test is called a mutation test or molecular analysis.

There are various different types of targeted therapy that work for different mutations.

Patients whose tumours test positive for these mutations, and who have been given matched targeted treatments, gain more benefit than from standard chemotherapy, a treatment they may also get at a later date.

In addition, we know that people without a mutation do not respond to targeted treatments as well.

Targeted therapies differ from standard chemotherapies in several ways:

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<thead>
<tr>
<th>Targeted therapies</th>
<th>Chemotherapies</th>
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<tr>
<td>• work on <strong>specific</strong> targets associated with cancer</td>
<td>• work on <strong>all</strong> rapidly-dividing normal and cancerous cells</td>
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<tr>
<td>• are specifically chosen or designed to affect their target</td>
<td>• are identified because they kill cells</td>
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<tr>
<td>• block cells from multiplying</td>
<td>• kill tumour cells</td>
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The most common mutations of non-small cell lung cancers are called:

- epidermal growth factor receptor (EGFR)
- anaplastic lymphoma kinase (ALK), and
- ROS1

These mutations lead to uncontrolled cell growth and tumour formation, and targeted therapy drugs aim to interrupt this.

EGFR, ALK and ROS1 are only three of the many identified cancer cell mutation types and are currently (February 2019) the only ones with available approved drug treatments in the UK.

For people who are found to have advanced non-small cell lung cancer, further tests are likely to be carried out to see if the cancer also showed the EGFR, ALK or other mutations. This is to make sure treatment begins with the one that is most effective for you. This would be your first line treatment.

**How is molecular analysis done?**

The same tissue biopsy used to make the original diagnosis of lung cancer often has enough left-over cancer cells to do the molecular analysis to check for mutations.

However, if this is not the case, or the biopsy is unsuitable, your doctor may recommend another biopsy.

While the biopsy procedure itself may be completed in just a few minutes, the process of examining the results can take a few days, or even two or three weeks. This can be worrying so it can help to ask your doctor at the outset about how long it is likely to be for you.
Treating lung cancer with a targeted therapy

Why am I getting a targeted therapy?
If you are being offered a targeted therapy, this is because:

- your lung cancer is inoperable or not otherwise radically treatable (treated with an intent to cure)
- tests have shown that you have a type of lung cancer that responds well to it, and
- your doctor thinks it is right for you

Depending on your situation, and the type of cancer you have, targeted therapy may be the first treatment you receive, known as first line treatment, or be as a subsequent second or third line treatment.

Are there any alternative treatments available to me?
Yes, chemotherapy can also be used as a first or second treatment for lung cancer. Chemotherapy does not depend on the presence of mutations in the cancer tissue the way targeted therapies do.

Some people may receive one of the new immunotherapy drugs, or even combinations of chemotherapy and immunotherapy.

“I remember when the oncologist told me I had been matched up to the new drug and I would need to only take one tablet a day and would not need any chemo, I jumped up and gave the man a big hug.”

Eric
Which targeted therapies can be used?
There are several types of targeted therapy licensed to treat lung cancer. Each drug has both a drug name and a brand or trade name.

Drugs currently used to treat lung cancer in the UK are:

- afatinib (brand name Giotrif®)
- erlotinib (brand name Tarceva®)
- gefitinib (brand name Iressa®)
- osimertinib (brand name Tagrisso®)
- ceritinib (brand name Zykadia®)
- crizotinib (brand name Xalkori®)
- alectinib (brand name Alecensa®)
- nintedanib (brand name Vargatef®)

All these drugs belong to a group of drugs known as tyrosine kinase inhibitors (TKIs). They work by blocking certain chemical processes that tell cancer cells to grow, divide and spread.

Afatinib, erlotinib, gefitinib, and osimertinib are EGFR inhibitors, and crizotinib, ceritinib and alectinib are ALK inhibitors. Crizotinib may also be used to treat people with ROS1 mutation.

Nintedanib blocks certain adenocarcinoma cell activity and is given in combination with a chemotherapy drug, docetaxel (brand name Taxotere®), after first line chemotherapy.

Targeted therapy treatments for lung cancer are continually developing. There are many clinical trials underway around the UK, and internationally, looking at the best way to treat lung cancer using targeted therapy. Other targeted therapy drugs currently being researched for lung cancer include brigatinib and lorlatinib (both ALK inhibitors).
Will these drugs be available to me?

Not all targeted therapies licensed to treat non-small cell lung cancer are currently available as a standard treatment on the NHS. When a new drug gains a European licence it is available to buy and use as a treatment in the UK. However, NHS doctors are only allowed to use drugs which have been approved by either National Institute for Health and Care Excellence (England and Wales) or Scottish Medicines Consortium (Scotland), or are pending a decision by NICE about routine commissioning (England).

These organisations look at a combination of how well a drug works and the cost of using the drug. They then compare it to other available drugs used for the same health problem. Unfortunately this can lead to variations in the availability of these drugs on the NHS, depending on which country in the UK you live in and whether or not they have been approved for use on the NHS.

If a drug has a European licence, it may be available to you through a private health insurance scheme if you have one. Although not an option for many people, having this licence may also mean the drug could be available for you to buy yourself. Otherwise, the drug may be available through the Early Access to Medicines Scheme, or as part of a clinical trial, or through compassionate use.

In some circumstances, you may be able to make voluntary financial contributions, also known as top-up payments, towards the cost of an available treatment not currently funded by the NHS.

In each case, speak to your cancer doctor before going ahead with these treatments.
Receiving a targeted therapy treatment

How do you take a targeted therapy?
Targeted therapy drugs for non-small cell lung cancer come as a tablet, which you take by mouth, every day, at home. You should take them at the same time/s each day.

It is very important that you take the tablets according to the instructions your cancer doctor or pharmacist has given you.

Taking extra doses of some medicines can be harmful. In some cases even one extra dose can cause you problems. If you take extra doses of your medicine by mistake, you must tell your cancer doctor straight away.

You can keep taking a targeted therapy for as long as it keeps working for you.

Can I take the targeted therapy with other medicines or herbal remedies?
Some other medicines can be harmful to take at the same time as a targeted therapy.

Tell your cancer doctor or lung cancer nurse specialist about any other medicines you take. This includes prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

Your cancer doctor may change the dose or choose different medicines while you are taking a targeted therapy.
**Do targeted therapies have side effects?**

All forms of cancer treatment have side effects of one sort or another. Many people experience very few side effects with a targeted treatment. However, some people may develop severe side effects that require the treatment to be stopped or the dose lowered.

Side effects can make living with your illness more difficult, however most people find ways to help them cope.

While some of the side effects listed below may sound alarming, the main things is for you to be aware of how you are feeling and to speak to your medical team if you are worried.

Your doctors will also tell you about any potentially serious side effects of your treatment to be aware of as they may need urgent attention.

<table>
<thead>
<tr>
<th>Targeted therapy</th>
<th>Common side effects (affects more than 10 in every 100 people)</th>
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| Afatinib (brand name Giotrif®) | **Most common side effects:**  
1. Diarrhoea. This is most likely to start within the first two weeks of taking afatinib.  
2. Rash and acne-like skin conditions which may be dry and itchy. Avoid being out in the sun and moisturise your skin regularly. Your lung cancer nurse specialist will be able to give you advice about this.  
**Other very common side effects:**  
• Infection of the nail and surrounding area.  
• Reduced appetite.  
• Nosebleeds.  
• Inflammation of the lining of the mouth. |
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| Erlotinib (brand name Tarceva®) | **Most common side effects:**  
1. Rash and other skin changes which may be dry and itchy. Most often on your face, upper chest, and back. Avoid being out in the sun and moisturise your skin regularly. Your lung cancer nurse specialist will be able to give you advice about this.  
2. Diarrhoea. This is most likely to start within the first week or two of taking erlotinib.  
**Other very common side effects:**  
• Abnormal blood tests for the liver function.  
• Cough.  
• Depression.  
• Difficulty in breathing.  
• Feeling or being sick.  
• Fever.  
• Hair loss.  
• Headache.  
• Infection.  
• Loss of appetite and decreased weight.  
• Rigors (sudden feeling of cold and shivery with a rise in temperature).  
• Skin sensation or numbness in the extremities.  
• Sore mouth.  
• Stomach pain, indigestion and flatulence (wind).  
• Tiredness. |
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</table>
| Gefitinib (brand name Iressa®) | **Most common side effects:**  
1. Rash and other skin changes which may be dry and itchy. Most often on your face, upper chest, and back. Avoid being out in the sun and moisturise your skin regularly. Your lung cancer nurse specialist will be able to give you advice about this.  
2. Diarrhoea. This is most likely to start within the first week or two of taking gefitinib.  
**Other very common side effects:**  
• Dry, red or sore mouth.  
• Feeling or being sick.  
• Loss of appetite.  
• Increase of a liver enzyme called alanine aminotransferase in a blood test; if too high, your cancer doctor may stop your treatment.  
• Weakness. |

“I was advised there may be some side effects with the targeted therapy I am taking. I have had a rash but have managed to cope with it by using creams my doctor has given me.”  

Margaret
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<tr>
<th>Targeted therapy</th>
<th>Common side effects (affects more than 10 in every 100 people)</th>
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<tr>
<td><strong>Osimertinib</strong></td>
<td><strong>Most common side effects:</strong></td>
</tr>
<tr>
<td>(brand name</td>
<td>1. Diarrhoea – this may come and go during treatment.</td>
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<tr>
<td>Tagrisso®)</td>
<td>Tell your doctor if your diarrhoea does not go away or becomes severe.</td>
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<td></td>
<td>2. Skin and nail problems – signs may include itching, dry skin, rash, redness around the fingernails.</td>
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<td></td>
<td><strong>Other very common side effects:</strong></td>
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<td></td>
<td>• Inflammation of the inner lining of the mouth.</td>
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<tr>
<td></td>
<td>• Abnormal decrease in the number of white blood cells.</td>
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<td></td>
<td>• Reduction in the number of platelets in the blood.</td>
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<tr>
<td><strong>Ceritinib</strong></td>
<td><strong>Most common side effects:</strong></td>
</tr>
<tr>
<td>(brand name</td>
<td>1. Diarrhoea. If this symptom becomes severe, you should tell your cancer doctor immediately.</td>
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<tr>
<td>Zykadia®)</td>
<td>2. Feeling or being sick.</td>
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<td></td>
<td><strong>Other very common side effects:</strong></td>
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<td></td>
<td>• Stomach ache.</td>
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<td>• Decreased appetite.</td>
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<td>• Constipation.</td>
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<td></td>
<td>• Abnormal results from blood tests to check kidney and liver function.</td>
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<td></td>
<td>• Rash.</td>
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<td></td>
<td>• Anaemia (low red blood cell count).</td>
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<td></td>
<td>• Heartburn.</td>
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<td>Regular heart function tests may be made.</td>
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| Crizotinib (brand name Xalkori®) | **Most common side effects:**  
1. Eyesight problems. Seeing flashes of light, blurred vision, or double vision, often beginning soon after starting treatment. Tell your cancer doctor straight away if you experience this.  
2. Feeling or being sick and diarrhoea.  
**Other very common side effects:**  
• Abnormalities in liver blood tests.  
• Change in sense of taste.  
• Constipation.  
• Dizziness.  
• Leukopenia (reduction of white blood cells which are important in fighting infection).  
• Neuropathy (feeling of numbness or pins and needles in the joints or muscles).  
• Oedema (excess fluid in body tissue, causing swelling of the hands and feet).  
• Reduced appetite.  
• Tiredness.  
• Oesophageal (gullet) disorders. |
### Targeted therapy

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<tr>
<td>Alectinib</td>
<td><strong>Most common side effects:</strong></td>
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<tr>
<td>(brand name Alecensa®)</td>
<td>1. Abnormal results of blood tests to check for liver problems or muscle damage. 2. Feeling tired, weak or short of breath due to a reduction in the number of red blood cells <em>anaemia</em>).</td>
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<tr>
<td></td>
<td><strong>Other very common side effects:</strong></td>
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<tr>
<td></td>
<td>• Being sick – if you are sick after taking the medication, do not take an extra dose, just take your next dose at the usual time.</td>
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<tr>
<td></td>
<td>• Constipation.</td>
</tr>
<tr>
<td></td>
<td>• Diarrhoea.</td>
</tr>
<tr>
<td></td>
<td>• Feeling sick (<em>nausea</em>).</td>
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<tr>
<td></td>
<td>• Rash.</td>
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<tr>
<td></td>
<td>• Swelling caused by fluid build-up in the body (<em>oedema</em>).</td>
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<td></td>
<td>• Weight gain.</td>
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<tr>
<td>Targeted therapy</td>
<td>Common side effects (affects more than 10 in every 100 people)</td>
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<td>------------------</td>
<td>---------------------------------------------------------------</td>
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</tbody>
</table>
| **Nintedanib** (brand name Vargatef®) | **Most common side effects:**
| | 1. Diarrhoea. If this symptom becomes severe, you should tell your cancer doctor immediately.
| | 2. Decreased appetite.
| | **Other very common side effects:**
| | • Feeling sick or being sick.
| | • Numbness or tingling in fingers and toes.
| | • Stomach pains.
| | • Liver changes.
| | • Rash, or red, dry, itchy skin. |

The above information on side effects is taken from Summary of Product Characteristics (SPC), which is provided for each drug, as detailed in the electronic Medicines Compendium (eMC). For further information about drug side effects please go to [www.medicines.org.uk](http://www.medicines.org.uk).
Practical tips for managing common side effects
While this information will help you manage side effects, it is still important that you talk to your cancer team if you experience any of them when you start your treatment.

Breathing difficulties/infection
If you have breathing difficulties, a cough or high temperature (37.5°C or higher), you need to contact your cancer doctor or lung cancer specialist nurse for urgent advice.

Diarrhoea
• There are anti-diarrhoea medications, which can help to reduce diarrhoea in most people.
• Take small sips of liquids (such as sports drinks without sugar) often throughout the day.
• Eat mild food, such as toast and crackers.
• Limit spicy foods.

Feeling or being sick
• There are very powerful anti-sickness drugs, which can help reduce sickness in most people.
• The type of food that you eat or smell may make you feel worse.
• Drink plenty of fluids.
• If the sickness continues, speak to your cancer doctor or lung cancer nurse specialist.

Rash and other skin problems
• Moisturise your skin regularly. Your lung cancer nurse specialist will advise which creams are best for you.
• Avoid being out in hot sun.
• Use a sunscreen of SPF 30 or higher, preferably containing zinc oxide or titanium dioxide.
• Wear a hat in the sun.
• Avoid over-the-counter spot-related treatments, including products with benzoyl peroxide.
• Remove any dermatologist-approved makeup with a gentle liquid cleanser.

Tiredness/breathlessness
• If you feel breathless, your legs ache or you are concerned that you feel too tired, ask your cancer doctor or lung cancer nurse specialist for advice.
• A small amount of regular exercise will also help reduce your tiredness.
• Make time for activities that help you relax.
• If you are feeling breathless, planning ahead will help to reduce the energy you spend on everyday activities.

Please see our Managing your lung cancer diagnosis and Managing lung cancer symptoms booklets for more information on managing side effects. See page 2 for details on how to get a copy.

You will be given a contact phone number to phone if you experience difficulties with side effects.

This number should be used at times when it may be difficult to contact your lung cancer nurse specialist or cancer doctor, such as during the night or at the weekend.

Lung cancer nurse specialist
Name:
Phone number:
Other contact phone number:
How do the doctors know if the targeted therapy is working?
It can take some time to assess how targeted treatments are working, though you may be aware of changes or reduction in symptoms. When you start your treatment, you will get dates set for follow-up appointments. You may have a CT scan or X-ray to help assess what is happening.

If your symptoms have improved this may also suggest that the treatment is working, for example, less cough or breathlessness. If there is evidence that your cancer is responding to the targeted therapy then treatment will continue, as long as you are not having side effects which you can’t cope with.

If there is evidence that your cancer is not responding then it is important to know this, so that a decision on an alternative treatment can be made. Sometimes there will be no change in the state of your tumour when the X-ray or scan has been done. This may seem disappointing but is a worthwhile response, especially if you feel better.

Even if the targeted therapy has not changed the size of the tumour, it may well have delayed the growth.

“Taking a targeted therapy for me is an easy way to a kind of normality, considering that I am still battling lung cancer. Is a painless easy way to a normal life.”

Franca
How long will I stay on targeted therapy?
So long as your cancer continues to respond to the treatment, and any side effects you have are manageable, you are likely to keep getting the drug you are on.

Over time, as with many drugs, targeted therapies can lose their effectiveness. The cancer cells can develop a resistance to the drugs, and this represents one of the main challenges to effective treatment.

For example, cancer treated with crizotinib is likely to develop a resistance to it over time. At this point, treatment may change to ceritinib. Cancers can develop “new” mutations that make targeted therapy drugs ineffective. In some cases, new drugs are being developed to overcome these mutations.

Other treatment options may be available to you, and your cancer doctor will be able to tell you about these if they become approved for use.

Future developments in targeted therapy
Research is taking place to investigate how cancer cells become resistant. It is also developing and testing new drugs to combat this resistance. For example, one of the earliest EGFR resistance mutations identified following treatment with erlotinib or gefitinib is known as T790M. The drug osimertinib (brand name Tagrisso®) has now been approved as a treatment when this change is identified.

As things move forward, a great deal of research is looking at these mechanisms in detail. It may be that if your treatment becomes less effective, doctors may be able to take another look at your cancer through a biopsy to see what is happening.
Questions to ask your doctor or lung cancer nurse

Before choosing a targeted therapy as a treatment option, you should understand the expected benefits, side effects, and risks. Ask your cancer doctor or lung cancer nurse specialist these questions on your next visit. Learn as much as you can about your treatment, and get an idea of the expected outcome.

1. What type of targeted therapy will I be getting?

2. What is the aim of the targeted therapy?

3. Are there other types of treatment that could be suitable for me instead of a targeted therapy?

4. What are the risks and side effects of the targeted therapy I will be taking? How do these side effects compare with side effects of other treatments?

5. How long will I have to wait before starting treatment?

6. How will I know if the targeted therapy is working?

7. What can I do to prepare for treatment and reduce the chance of side effects?

8. Will I need to change my lifestyle in any way?

9. If this targeted therapy doesn’t work, are there other treatments I can get?

10. Are there any clinical trials I would benefit from?
About our lung cancer information

All of our information is written either by our information team or by lung cancer experts. We have a panel of lung cancer experts made up of doctors, nurse specialists and other health professionals involved in the care of people affected by lung cancer. These people help us on a voluntary basis. You can find out about our Expert Panel at www.roycastle.org/expertpanel

Our information is also reviewed by members of our Reader Panel (made up of people who have experience of lung cancer). This ensures that our lung cancer information meets their needs. You can find out about our Reader Panel at www.roycastle.org/readerpanel

Our information is accredited by The Information Standard, which makes sure that it is trustworthy, easy to read and reliable. It also must be based on the best clinical evidence that is available.

The information is evidence based and follows national clinical guidelines for the management of lung cancer. You can find references to sources of information within this booklet at www.roycastle.org/evidence

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We value your feedback
If you would like to tell us what you think about this information booklet or would like to join our Reader Panel and review our lung cancer information, please e-mail us at info@roycastle.org
Roy Castle Lung Cancer Foundation is the charity that gives help and hope to people affected by lung cancer. The charity has two aims – supporting people living with lung cancer and saving lives.

**Supporting people living with lung cancer**
Working closely with lung cancer nurses, we provide information, run lung cancer support groups and offer telephone and online support. Our patient grants offer some financial help to people affected by lung cancer.

**Saving lives**
We fund lung cancer research, campaign for better treatment and care for people who have lung cancer, and raise awareness of the importance of early diagnosis. Our lung cancer prevention work helps people to quit smoking and encourages young people not to start smoking.

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**Contact us**
For more information, call our Lung Cancer Information and Support Services:

0333 323 7200 (option 2)

or visit our website: [www.roycastle.org](http://www.roycastle.org)

**Head Office**
Cotton Exchange Building,
Old Hall Street
Liverpool, L3 9LQ

**Email:** foundation@roycastle.org

**Information and Support Services**
98 Holm Street,
Glasgow G2 6SY

**Email:** info@roycastle.org

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*Expect Better*

Roycastlelungcancer  
@Roy_Castle_Lung

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