Immunotherapy and lung cancer

GLOBAL LUNG CANCER COALITION

What is the immune system?

Our immune system is designed to protect us from damage mainly by viruses and bacteria. In doing this, it is important that it should be able to recognise what is a normal part of our own body and abnormal or foreign cells or germs. The immune system has evolved in human development to be really quite amazing in its functions.

When it recognises the foreign material it can neutralise it with a special protein called an antibody or create a local area of inflammation that destroys the invader. Common vaccinations, for infections such as polio and tetanus, are designed to teach the immune system to respond very quickly if ever exposed to those germs so that serious illness never develops. Children born with serious malfunctions of the immune system suffer repeated infections in early childhood and can become seriously ill in the first year of life.

What prevents our immune system from attacking our own body?

We know how aggressive the immune system can be by just looking at the redness and swelling that occurs in response to a 'boil' or another skin infection. Because of the damage that it can do, it is important that the immune system be very well controlled and selective in what it attacks. Just as a warship might fly a flag in battle, so that it will not be hit by 'friendly fire', our cells have proteins on their surfaces that tell the immune system that they are normal and friendly. This recognition occurs when cells of the immune system bind with a protein of their own and this linkage of proteins turns off the immune response. This is referred to as an immune checkpoint. The normal tissue or part of the body should be left undamaged.

Some forms of arthritis and a variety of other serious conditions can occur when the immune system makes mistakes and attacks normal tissue – these are called auto-immune diseases.

Names and terminology

PDL-1 – a protein on normal tissue surface that the immune system will recognise as being normal and not foreign. Think of this as the flag that a warship might fly to identify itself as friendly.

PD-1 and CTLA-4 – proteins on immune system cells that will bind or stick to normal cell proteins and when this happens, the immune response is turned off. Think of these as the binoculars through which a sailor might recognise a friendly flag and tell the gunners to cease fire.

What does this have to do with tumours?

Tumours often have abnormal proteins on their outer surface that the immune system can identify and respond to. It is possible that this happens quite frequently and that the immune system destroys tumours at a small size so that they are never seen. Some tumours are however able to exploit the checkpoint system. They place some of these important proteins on their surface. Research has shown that these cancer cells disguise themselves, so they are not spotted by the checkpoints which mean the immune system does not destroy them.

At a biological level, how do these Immunotherapies work?

The new treatments work by allowing the immune system to destroy the 'foreign' tumour cells. If we think about the "false flag" and the "binoculars" some treatments will cover up the flag (on the tumour cell) whereas others cover up the equivalent of the binoculars on the tumour cell. The treatments, in this way, keep the immune cells "on" so they fight the cancer. They are specially designed immuno-globulins or antibodies that are given in a drip or an injection in the skin. They stick to their target like a limpet and are quite long-lasting.

Are there side-effects?

This is a very basic body system that is being manipulated. The aim is to re-invigorate the checkpoint system enough to allow tumour suppression without overdoing it so that auto-immune diseases can develop. This is a subtle balance and the current experience is that auto-immune disease involving the bowel, lung or other body organs is seen in some patients on these treatments. If you have such a treatment your doctor will be carefully looking for known and new side-effects.

How do new treatments develop?

When any new cancer treatment is being explored it goes through a series of tests and research trials. This is a process that can take a number of years, but the scientists working on new discoveries, cancer specialists and the Government bodies who approve new medicines do their best to make new medicines available as soon as possible after they are proven effective and safe.

The research and approval process can take a number of years. This careful evaluation is required to test a number of things:

- Does the drug do the good things that it is intended to do? In this case does it have a positive effect on the lung cancer?
- Does it allow patients with cancer to live longer?
- Does it improve symptoms and quality of life considering the benefits of tumour suppression together with any side-effects?
- Are there side effects with the new drug? Are they frequent? Are they severe?
- Is the new drug better than any existing therapy?

In short, this process is one of discovering what are the risks and what are the benefits. This may be the usual or standard treatment such as chemotherapy, or may be a placebo or dummy treatment if there is no further standard treatment available for the patient at that stage of their cancer journey.

Placebo treatment will only ever be approved by an Ethics Committee where it is unclear that the study treatment is better or safer than no treatment at all.

What immunotherapy research is happening?

Initially, research with immunotherapy was undertaken in patients with advanced melanoma (an aggressive form of skin cancer). The results looked positive – with shrinkage of tumours in patients where other treatments were ineffective. Research was then extended to lung cancer. Research is looking at the use of these drugs on their own and also if they can work better in combination with other treatments. Some immunotherapy drugs have already been approved and others are currently being researched.

Can immunotherapy help me?

Patients wondering if immunotherapy would enhance their treatment should discuss it with their clinical team. Some current treatments or trials are for patients who have already had some initial treatment (whether surgery, chemotherapy or radiotherapy) and where there are signs that their lung cancer is active again and is spreading. There are other trials involving people who have not had any other treatment. Clinical trials are carefully designed and therefore not all patients will be suitable for clinical trials. Your clinical team will be able to discuss trials that might be relevant to you and if suitable, how you can participate.

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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 2 – February 2016.