

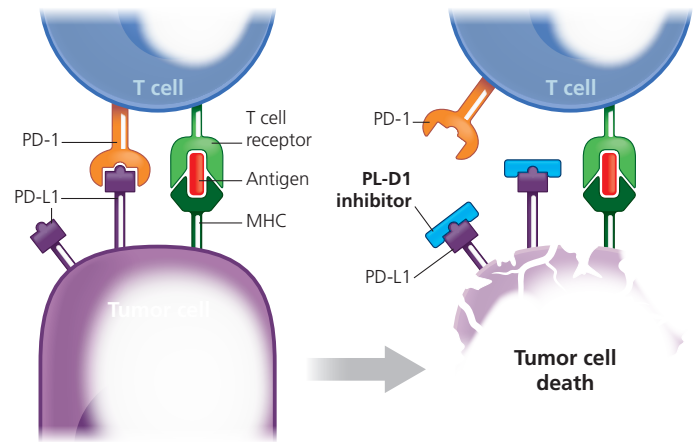
When checkpoint inhibitor therapy treatment stops working... what's next?

What is checkpoint inhibitor therapy?

This is a type of **immunotherapy**, using the body's immune system to fight cancer. It's sometimes called **immuno-oncology** (I-O) treatment.

As part of a normal immune system, 'immune checkpoint' proteins stop the immune system overreacting and attacking healthy body cells. Some cancer cells hide from the immune system by making large amounts of one of these proteins.

An immune checkpoint inhibitor blocks the protein the cancer cells make (PD-L1 for example), allowing immune system cells called T cells to recognize and attack them.



PD-L1 inhibitors block PD-L1, enabling T cells to find and kill cancer cells

Why can the treatment fail?

For some patients, this type of treatment works really well, but for others it doesn't work at all. In these patients, the cancer cells are **naturally resistant** to this type of treatment. They may have gene changes (mutations) that help stop T cells from targeting the tumor or the tumor may have ways of switching the T cells off.

Other people's tumors may become resistant to treatment after a while and their cancer begins to grow again. The treatment may have killed the cancer cells that are susceptible to it, leaving behind only naturally resistant cancer cells.

Sometimes the treatment helps to stop the cancer growing but the **side effects** are unmanageable. If this happens, your doctor may stop the treatment for a while so you can recover from the side effects.

What happens if checkpoint inhibitor treatment doesn't work for me?

If your tumor starts growing again, it may be possible for the immunotherapy to be combined with one or more other drugs, although this approach is not well studied. If the cancer hasn't progressed much, your doctor may suggest surgery or radiotherapy to deal with any areas of cancer progression.

Researchers are looking into adding other types of therapies to checkpoint inhibitor treatment, to help it to work. Your doctor may suggest a clinical trial, combining the checkpoint inhibitor treatment with chemotherapy, for instance.

Standard treatment options can be limited if a tumor has already been treated with immunotherapy and chemotherapy, but additional chemotherapy-based treatment may be helpful. Other treatments being researched include targeted therapies and cancer vaccines. Targeted therapies work by blocking the chemical signals that encourage cancer cells to divide and grow.

Information and support

You may need support from elsewhere, as well as from your doctors and nurses. Some organizations and most large **cancer charities** run information services online and/or by phone. This includes the American Cancer Society (cancer.org) in the USA, Cancer Research UK (cancerresearch.org.uk), and The Cancer Council in Australia (cancer.org.au/).

Ask your nurse about local support or patient advocacy groups. There are also now many online forums, such as **KRAS Kickers** (www.kraskickers.org/), **Macmillan Cancer Support** (community.macmillan.org.uk), **LungCancer.Net** (lungcancer.net/forums), and **Lungevity** (forums.lungevity.org/forum/15-nscl-group/).

Clinical trials

There may be a clinical trial of a new treatment for your cancer that you can join. All potential treatments that show promise in early tests need to enter clinical trials.

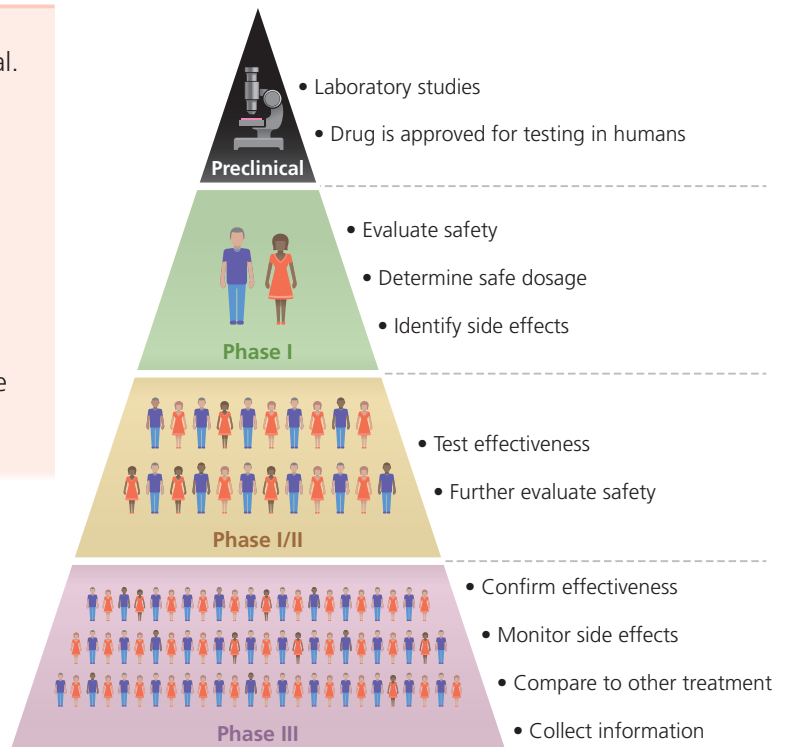
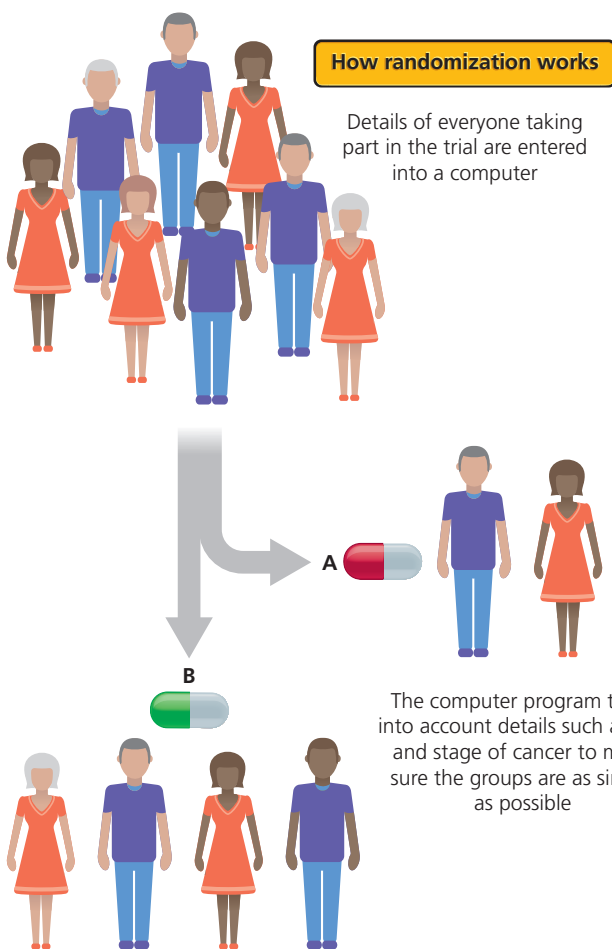
About clinical trials

New treatments must go through several phases of clinical trial before they can be submitted for approval.

Phase I trials look at side effects of potential new treatments and make sure they are safe. Everyone taking part has the trial treatment.

Phase II trials show whether the new treatment has promise, and for which types of cancer.

Phase III trials include participants with a specific cancer type and stage. They test whether the new treatment gives better results than the current best standard treatment. One-half of the participants have the new treatment and the other one-half have the standard treatment.



What happens in a trial?

Trials that compare two or more treatments are usually **randomized**. The participants are allocated to trial groups. Neither they, nor their doctor can choose which group they're in.

Another way of making sure trials get reliable results is to set **eligibility criteria** (certain conditions you must fulfil to enter them). These often include a specific type and stage of cancer, treatment you've already had, and other medical conditions.



Ask your doctor

- What treatment can you offer if checkpoint inhibitor therapy stops working?
- Will adding another type of treatment help checkpoint inhibitor therapy to work?
- What can you do to help with my treatment side effects?
- What types of treatment are most suitable for me now?
- Are there any trials I could enter that are for my type and stage of cancer?
- What are the possible advantages and risks of taking part in a trial?
- What will I have to do if I join a trial?
- Will taking part in a trial affect my medical insurance?
- Will there be any help to cover costs and how much time will it take up?

How do I find a clinical trial?

Your doctor has all the information about your tests and past treatments, so ask whether they know of any trials that may be suitable – and which you may be eligible for.

You may also be able to find clinical trials online. How you do this depends to some extent on where you live. There are cancer **clinical trials databases** based in the UK (cancerresearchuk.org/about-cancer/find-a-clinical-trial), Europe (eortc.org/clinical-trials-database/), and the USA (clinicaltrials.gov).