Checkpoint inhibitors

This information is about checkpoint inhibitors, a type of targeted drug used in the treatment of certain types of lymphoma.

On this page

What are checkpoint inhibitors?
Who can have them?
Benefits
How are they given?
Possible side effects
Precautions

What are checkpoint inhibitors?

Checkpoint inhibitors are a type of targeted treatment that use your own immune system to try to destroy lymphoma cells.

Lymphocytes are white blood cells that are part of your immune system. Your body produces lymphocytes to help you fight infection and disease, including cancer. There are different types of lymphocytes, including T lymphocytes (T cells) and B lymphocytes (B cells), and these have different roles in your immune system. In cancer, cells that become abnormal are not detected by your immune system and can grow out of control. Any type of cell can become cancerous. In lymphoma, cancer develops when lymphocytes themselves become abnormal and are not detected and eliminated by your immune system.

Your T cells usually detect abnormal cells, including cancer cells, and get rid of them. All T cells have proteins called ‘T-cell receptors’ on their surface, which bind (attach) to other proteins (sometimes called ‘antigens’) on other cells. When your T-cell receptors bind to another cell, they can ‘turn on’ your immune system, making it destroy the cells.

T cells also have a different kind of protein that acts as an ‘off switch’. These proteins are very important in helping your T cells identify normal, healthy cells, so they do not destroy them. One of these ‘off switches’ is a protein called ‘programmed death-1’
(PD-1). PD-1 binds (sticks) to a protein called ‘programmed death-1 ligand’ (PD-L1) on normal cells, and this interaction (the ‘checkpoint’) tells the T cell not to destroy the normal cell.

If your own cells become abnormal, they are usually recognised as different by T cells and destroyed by your immune system. Some cancer cells produce PD-L1, which makes them look like normal, healthy cells. The interaction between PD-L1 on the cancer cell and PD-1 on the T cell helps cancer cells avoid being killed by your immune system.

**Figure: The PD-1/PD-L1 immune checkpoint with a cancerous, tumour cell**

Checkpoint inhibitors work by blocking the PD-1/PD-L1 ‘checkpoint’ and therefore blocking the ‘off-switch’ for the T cell. This allows the T cells to recognise the lymphoma cells as abnormal, and your immune system can then destroy the lymphoma cells.

**Figure: The checkpoint inhibitor blocks the PD-1/PD-L1 immune checkpoint**

There are two checkpoint inhibitors currently approved for use for people with lymphoma in Europe:

- nivolumab (Opdivo®)
- pembrolizumab (Keytruda®).
Both of these drugs bind to PD-1 and block the checkpoint, allowing cancer cells that have PD-L1 to be destroyed by your immune system.

Drugs that block other checkpoints are also in development.

**Who can have them?**

Both nivolumab and pembrolizumab are approved in Europe to treat some people with classical Hodgkin lymphoma who have already had other treatments. They are also used to treat some other cancers.

- Nivolumab and pembrolizumab are each recommended for people with classical Hodgkin lymphoma that has relapsed or progressed (got worse) after an autologous stem cell transplant and a different type of targeted treatment, brentuximab vedotin.
- Pembrolizumab can also be used for people with classical Hodgkin lymphoma who cannot have an autologous stem cell transplant and who have already had brentuximab vedotin.

Checkpoint inhibitors are being tested in further clinical trials in people with this type of lymphoma, for example to be used earlier in the treatment pathway. Other checkpoint inhibitors are also being developed and tested. Use our searchable database to see if there is a clinical trial that might be suitable for you at Lymphoma TrialsLink.

**Are they available on the NHS in the UK?**

Nivolumab and pembrolizumab have been assessed by health authorities for some uses on the NHS in the UK. They are currently only available on the NHS for some people in certain parts of the UK.

**In Scotland**

- Nivolumab is available on the NHS for people with relapsed or refractory classical Hodgkin lymphoma who have had an autologous stem cell transplant and brentuximab vedotin.
- Pembrolizumab is available on the NHS for people with relapsed or refractory classical Hodgkin lymphoma who have had brentuximab vedotin and a stem cell transplant. It can also be used for people who have had brentuximab vedotin but can’t have a stem cell transplant. Pembrolizumab can only be given for up to 2 years.
In England and Wales

- Nivolumab is available on the NHS for people with relapsed or refractory classical Hodgkin lymphoma who have had an autologous stem cell transplant and brentuximab vedotin.

Northern Ireland usually follows NICE recommendations.

In England, pembrolizumab is available through the Cancer Drugs Fund for people with relapsed or refractory classical Hodgkin lymphoma who have had brentuximab vedotin and can’t have a stem cell transplant. Pembrolizumab can only be given for up to 2 years.

Benefits

Results from the main trials that led to approval of nivolumab and pembrolizumab are briefly described below.

Benefits of nivolumab

In several clinical trials, around two-thirds of people with relapsed or refractory classical Hodgkin lymphoma responded to nivolumab (their lymphoma shrank or disappeared completely).

Benefits of pembrolizumab

In a clinical trial of 210 people with relapsed or refractory classical Hodgkin lymphoma, around two-thirds of people responded to pembrolizumab.

How are they given?

You have nivolumab as an intravenous infusion (into a vein) over 60 minutes. You usually have the treatment once every 2 weeks, where each 2-week period is a ‘cycle’ of treatment. Most people can have the treatment in hospital as an outpatient, but some people might need to stay overnight for monitoring. It takes an average of 2 months before the benefits of nivolumab are seen. You continue to have nivolumab long-term to keep your lymphoma under control. You can stop treatment if your lymphoma stops responding or you develop side effects that are bad enough to make you stop it.

Pembrolizumab is given in a similar way to nivolumab but the infusion takes 30 minutes and it is usually given once every 3 weeks. You can usually continue to have treatment for up to 2 years if you are being treated on the NHS. You can stop
treatment earlier if your lymphoma stops responding or your side effects are not manageable.

Possible side effects

All medicines can cause side effects (unwanted effects of treatment). As nivolumab and pembrolizumab are new treatments, more information about possible side effects is still being gathered.

The most common side effects of both drugs, which can affect more than 1 in 10 people, are:

- digestive problems, such as diarrhea and nausea
- rash and itching
- fatigue (extreme tiredness).

These side effects are not usually severe.

Immune-related side effects can occur, due to the immune system causing inflammation of your organs. These can include problems with your lungs, bowel, liver, kidneys and thyroid. These side effects can usually be treated with steroids or go away when you stop treatment with checkpoint inhibitors. In some cases, problems can be severe and some people take a long time to recover.

Severe infusion-related reactions (occur while the treatment is given or shortly afterwards) can develop that make people feel very ill and require prompt treatment. Symptoms of infusion reactions include fever, chills, shaking, dizziness and itching. If you have an infusion reaction, you are monitored carefully and the checkpoint inhibitor treatment might be stopped.

This is not a complete list of side effects that have been reported. Ask your medical team for the most up-to-date information about possible side effects. Ask all the questions you have. You also need to tell your medical team about any other conditions you have and any medicines, supplements or complementary therapies you are taking before you start any new treatment.

Your medical team monitor you closely for side effects during treatment. They can tell you what to look out for and who to contact if you have any problems.

Precautions

You might not be able to have checkpoint inhibitors if you are taking other medications or have other conditions.
Make sure you tell your doctor about any medical conditions and any medicines you are taking.

Your doctor may reduce your dose and monitor you more closely or recommend that you do not have checkpoint inhibitors if you have problems such as autoimmune conditions (where your body attacks itself) or serious lung problems. Your doctor might also change your dose if you experience troublesome side effects.

Checkpoint inhibitors have not been approved for use in people under 18.

If you are pregnant, you should not usually have checkpoint inhibitors during pregnancy in case they could harm your unborn baby. You must use effective measures of contraception to prevent pregnancy during treatment and you should not breastfeed. Discuss your treatment options with your doctor if you think you might be pregnant.

References

The full list of references is available on request. Please email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

Acknowledgements

- With thanks to Dr Eve Gallop-Evans, Clinical Oncologist, Velindre Cancer Centre, Cardiff for reviewing this information.
- Dr Gallop-Evans has received advisory board honoraria, educational support and speaker’s fees from pharmaceutical companies including Takeda, Roche, Bristol Myers Squibb and Gilead.
- We would like to thank the members of our Reader Panel who gave their time to review this information.
Tell us what you think and help us to improve our resources for people affected by lymphoma. If you have any feedback, please visit [www.lymphoma-action.org.uk/Feedback](http://www.lymphoma-action.org.uk/Feedback) or email publications@lymphoma-action.org.uk.

All our information is available free of charge. If you have found it useful and would like to make a donation to support our work you can do so on our website [www.lymphoma-action.org.uk/Donate](http://www.lymphoma-action.org.uk/Donate). Our information could not be produced without support from people like you. Thank you.

**Disclaimer**

We make every effort to make sure that the information we provide is accurate at time of publication, but medical research is constantly changing. Our information is not a substitute for individual medical advice from a trained clinician. If you are concerned about your health, consult your doctor.

Lymphoma Action cannot accept liability for any loss or damage resulting from any inaccuracy in this information or third party information we refer to, including that on third party websites.

Neither the Information Standard scheme operator nor the scheme owner shall have any responsibility whatsoever for costs, losses or direct or indirect damages or costs arising from inaccuracy of information or omissions in the information published on the website on behalf of Lymphoma Action.