



Immune Checkpoint Inhibitors and Their Side Effects

An important part of the immune system is its ability to tell between normal cells in the body and those it sees as “foreign” (such as germs and cancer cells). This allows the immune system to attack the foreign cells while leaving normal cells alone.

Part of how the immune system does this is by using “checkpoint” proteins on immune cells. The checkpoints act like switches that need to be turned on (or off) to start an immune response. But cancer cells sometimes find ways to use these checkpoints to avoid being attacked by the immune system.

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Medicines known as [monoclonal antibodies](#) can be designed to target these checkpoint proteins. These drugs are called **immune checkpoint inhibitors** (or just **checkpoint inhibitors**).

Checkpoint inhibitors don't kill cancer cells directly. They work by helping the immune system to better find and attack the cancer cells, wherever they are in the body.

Medicines that target different checkpoint proteins are now used to treat many types of cancer.

All of these drugs can be given as an infusion into a vein (IV). Some of them can now be given as an injection under the skin (subcutaneously) over several minutes as well.

PD-1 and PD-L1 inhibitors

PD-1 is a checkpoint protein on immune cells called T cells. It normally acts as a type of “off switch” that helps keep the T cells from attacking other cells in the body. It does this when it attaches to PD-L1, a protein on some normal (and cancer) cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1, which helps them hide from an immune attack.

Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells.

PD-1 inhibitors

Examples of drugs that target PD-1 include:

- **Pembrolizumab (Keytruda)**
- **Nivolumab (Opdivo)**
- **Cemiplimab (Libtayo)**

PD-L1 inhibitors

Examples of drugs that target PD-L1 include:

- **Atezolizumab (Tecentriq and Tecentriq Hybreza)**
- **Avelumab (Bavencio)**
- **Durvalumab (Imfinzi)**

Both PD-1 and PD-L1 inhibitors have been shown to be helpful in treating many different types of cancer.

CTLA-4 inhibitors

CTLA-4 is another checkpoint protein on some T cells that acts as a type of “off switch” to help keep the immune system in check.

Ipilimumab (Yervoy) and **tremelimumab (Imjuno)** are monoclonal antibodies that attach to CTLA-4 and stop it from working. This can help boost the body's immune response against cancer cells.

These drugs are typically used along with a PD-1 or PD-L1 inhibitor. These combinations can be used to treat several types of cancer.

LAG-3 inhibitors

LAG-3 is a checkpoint protein on some types of immune cells that normally acts as a type of “off switch” to help keep the immune system in check.

Relatlimab is a monoclonal antibody that attaches to LAG-3 and stops it from working. This can help boost the body's immune response against cancer cells.

This drug is given along with the PD-1 inhibitor nivolumab (in a combination known as **Opdualag**). It can be used to treat melanoma of the skin, and it's being studied for use in several other types of cancer.

Side effects of checkpoint inhibitors

Some of the more common side effects of checkpoint inhibitors include:

- Diarrhea
- Fatigue
- Cough
- Nausea
- Skin rash
- Poor appetite
- Constipation
- Muscle and joint pain

Other, more serious side effects occur less often:

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting one of these drugs.



It's very important to report any new side effects to someone on your health care team as soon as possible. If serious side effects do occur, treatment may need to be stopped and you might be given high doses of corticosteroids to suppress your immune system.

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References



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