

## Types of Immune Checkpoint Inhibitors and its Side Effects

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### DESCRIPTION

An important part of the immune system is its ability to distinguish 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 and leave the normal cells alone. Part of how the immune system does this is by using "checkpoint" proteins on immune cells. Checkpoints act as switches that need to be turned on (or off) to initiate an immune response. But cancer cells sometimes find ways to use these checkpoints to evade the immune system's attack.

Drugs 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 do not kill cancer cells directly. They work by helping the immune system better find and attack cancer cells wherever they are in the body.

### PD-1 and PD-L1 inhibitors

PD-1 is a checkpoint protein on immune cells called T cells. It normally works as a type of "switch" to help prevent T cells from attacking other cells in the body. It does this when it binds 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 immune attack. Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and enhance 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)
- Avelumab (Bavencio)
- Durvalumab (Imfinzi)

Both PD-1 and PD-L1 inhibitors have proven useful in the treatment of many different types of cancer.

### CTLA-4 inhibitors

CTLA-4 is another checkpoint protein on some T cells that acts as a type of "switch" to help keep the immune system in check. Ipilimumab (Yervoy) is a monoclonal antibody that binds to CTLA-4 and stops its action. This can help boost the body's immune response against cancer cells. This drug is usually used together with a PD-1 inhibitor such as nivolumab. It can be used to treat skin melanoma and several other types of cancer.

### LAG-3 inhibitors

LAG-3 is a checkpoint protein on some types of immune cells that normally functions as a type of "switch" to help keep the immune system in check. Relatlimab is a monoclonal antibody that binds to LAG-3 and stops its action. This can help boost the body's immune response against cancer cells. This medicine is given together with the PD-1 inhibitor nivolumab (in combination known as Opdualag). It can be used to treat melanoma of the skin and is being investigated 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
- Rash
- Loss of appetite
- Constipation
- Muscle and joint pain

Other, more serious side effects occur less often:

**Infusion reaction:** Some people may have an infusion reaction while taking these medications. It is like an allergic reaction and can include fever, chills, facial flushing, rash, itchy skin, feeling dizzy, wheezing and difficulty breathing. It is important that you tell your doctor or nurse straight away if you have any of these symptoms while taking any of these medicines.

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**Auto-immune reponse:** By targeting a checkpoint protein, these drugs remove one of the safeguards of the body's immune system. Sometimes the immune system responds by attacking

other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone glands, kidneys, or other organs.