

Combined treatment with ipilimumab and nivolumab – Patient information

What kind of treatment is combined immunotherapy?

Ipilimumab (YERVOY®) is a monoclonal CTLA-4 antibody that plays a crucial role in regulating the body's natural immune system. When ipilimumab blocks this activity, the body's natural immune system is strengthened to successfully attack and fight cancer cells.

Nivolumab (PD-1 inhibitor, Opdivo®) is an antibody (a type of human protein) that acts against cancer cells by preventing/blocking them from binding to and activating PD-1 (a molecule in the body). If the cancer cells bind to PD-1, it will inhibit the immune system. Nivolumab therefore helps the body to reactivate the immune system and to fight the cancer cells.

Both nivolumab and ipilimumab have been approved in Norway for the treatment of melanoma (melanoma cancer) with metastasis. Clinical trials show better results by combining these two medications than giving them separately.

Treatment with nivolumab in combination with ipilimumab causes more serious side effects than if the medication is given separately.

Who can get the treatment?

Steroid treatment (Medrol®/prednisolone/dexamethasone®) is immune-inhibiting, and may reduce the effectiveness of ipilimumab and nivolumab. Therefore, there is an upper dose limit corresponding to a maximum of 10 mg of prednisolone per day. The treatment can be given to patients with melanoma metastasis, and who are in relatively good shape. The treatment cannot be given to pregnant women. It is best not to give the treatment to patients with HIV, active hepatitis or to patients who have treatment-intensive autoimmune diseases. Patients with brain proliferation can only receive treatment if they are asymptomatic and do not require steroids.

Ipilimumab + nivolumab treatment is administered as long as it is tolerated in a maximum of 4 courses at 3 weeks intervals. After this period, the patient will only get nivolumab, that will be administered

every 4 weeks for up to 2 years. In the event of serious side effects, one may decide to postpone the treatment or discontinue it altogether.

How can I prepare?

You should have a relatively new CT scan from the neck to the pelvis (possibly pet-CT). The examination is used as a basis for comparison of further disease evaluations. Some people also do an MRI scan of the head.

How is the treatment executed?

You must arrive one to two hours before the doctor's appointment on the day you will receive treatment, so that you can have blood tests done.

Before the start of the treatment, a needle is inserted into a vein on your arm.

- Ipilimumab is given by intravenous infusion for 60 minutes.
- Nivolumab is given as an intravenous infusion for 30 minutes.

The treatment is usually well tolerated, and you can return home after the treatment has ended.

The treatment with nivolumab and ipilimumab is given every 3 weeks for the first 4 courses, followed by nivolumab every 4 weeks for up to 2 years.

Side effects that may be useful to know in connection with this cure

You must expect one or more side effects from the treatment, and they may be from mild to more severe.

Please contact your doctor/hospital if you experience any of the symptoms below. It is IMPORTANT to get in contact as soon as possible, as the side effects are easiest to treat in the beginning.

Fatigue

Fatigue can be experienced on the treatment day, or sometimes a few days later.

Skin symptoms

- The treatment may cause a slight rash or redness on your skin. Your doctor may prescribe an ointment if your skin becomes irritated, and if it itches you can get anti-itching tablets. In case of a stronger rash, consult your doctor.

- Some people experience changes in skin and hair pigmentation (vitiligo). This is harmless, and has only cosmetic consequences.

Diarrhoea

- signs or symptoms of intestinal inflammation (colitis) that may worsen to bleeding or cause cavities in the intestine
- diarrhea (watery, loose or soft stools), vomiting or nausea
- increase in the number of bowel movements
- blood in the stool or stool of a darker color
- pain or tenderness in the abdomen, fever

Heavy breathing

Heavy breathing may be an expression of pneumonia:

- increased heavy breathing
- a newly formed cough

Headache

Persistent headaches for more than a day, possibly with reduced field of vision or "tender eyes", may be signs of pituitary/inflammation of the pituitary gland.

Other side effects

- hormonal disruptions
- hepatic impairment

Rare side effects

- weakness in legs, arms or face
- numbness or tingling sensation in the hands or feet
- increased tendency to bleed or to get bruises
- eye pain or reduced vision field

After treatment

The effect of the treatment will be checked every 3 months with CT from the neck to the groin, or pet-CT, some must also take MRI of the head.

The treatment is given as long as it is tolerated and as long as it is effective, but up to a maximum of 2 years.