

INFORMED CONSENT

Opdivo (Nivolumap)

Medication guide

Opdivo is a medicine that may treat your tumour by working with your immune system. In Germany it is approved for the use in melanoma. In Japan and the US it is approved for melanoma and non-small cell lung cancer. In all other tumour entities it is an „off-label use“.

What is the function of Opdivo?

A tumour develops many mechanisms to avoid an attack by the immune system. The efficacy of an immunotherapy with dendritic cells and the general immunological control of a tumour growth is controlled via certain immune checkpoints, among them the PD-1/PDL-1 pathway. Activated T cells are able to recognize and to destroy tumour cells. The receptor protein PD-1 is expressed on such activated T-cells. PDL-1 expressed on tumour cells delivers an inhibitory signal to activated T-cells upon binding to PD-1. The T-cells will be inactivated and thus are no longer able to attack the tumour. Opdivo is a monoclonal antibody that blocks the PD-1-receptor on T-cells. Therefore it prevents the binding of PD-1 to PDL-1 expressed on tumour cells. So this inhibitor drug Opdivo allows the T-cells to act against the tumour. Especially in combination with primed dendritic cell vaccination this is of importance due to the fact that after blockade of the PD-1 by Opdivo DC activated T-cells are able to attack the tumor.

Following specific problems can occur:

- **lung problems (pneumonitis)**

symptoms: new or worsening cough
 chest pain
 shortness of breath

- **intestinal problems (colitis)**

symptoms: diarrhea
 blood in your stools
 severe stomach pain

- **liver problems (hepatitis)**

symptoms: yellowing of your skin or in the whites of your eyes
severe nausea/vomiting
pain on the right side of your stomach area
drowsiness
dark urine
bleeding or bruise more easily than usual

- **kidney problems (nephritis, kidney failure)**

symptoms: decrease in the amount of urine
blood in your urine
swelling in your ankles

- **hormone gland problems**

symptoms: unusual headaches
extreme tiredness
weight gain or loss
changes in mood or behavior
hair loss
feeling cold
constipation
voice gets deeper

- **problems in other organs**

symptoms: rash
changes in eyesight
severe or persistent
muscle or joint pains
severe muscle weakness

Getting medical treatment right away may keep these problems from becoming more serious.

Before you receive Opdivo, tell your healthcare provider if you:

- have immune system problems such as Crohn's disease, ulcerative colitis or lupus, asthma, rheumatoid arthritis
- have had an organ transplant
- have lung or breathing problems
- have liver problems
- have any other medical conditions
- are pregnant or become pregnant
- are breastfeeding or plan to breastfeed

Opdivo can cause your immune system not only to attack the tumour but also normal organs and tissues of your body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead in rare cases to death. These problems may happen anytime during treatment or even after your treatment has ended.

How do you receive Opdivo?

- Your healthcare provider will give you Opdivo into your vein through an intravenous line (i.v.) over 60-90 minutes. In the combination with dendritic cell vaccination Opdivo is usually given every 4 weeks within the week prior to the vaccination.
- Your healthcare provider will decide how many treatments you need.

I agree with the Opdivo treatment including the „off-label use“.

I have no further questions.

Date

Patient's signature

Doctor's signature