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Opdualag® (active substances: nivolumab, relatlimab)

First authorisation in Switzerland: 23 December 2022

Medicinal product (concentrate for solution for infusion) for the first-line treatment of adults with melanoma with PD-L1 expression below 1%

About the medicinal product

The medicinal product Opdualag contains two monoclonal antibodies (immunologically active proteins): nivolumab and relatlimab.

Opdualag is used to treat adults with melanoma that cannot be removed by surgery (non-resectable) or has spread (metastatic) with a PD-L1 expression below 1%.

Opdualag was authorised in connection with "Project Orbis". Project Orbis is a programme for promising cancer treatments coordinated by the FDA, the US regulatory authority. It provides a framework for the concurrent submission and review of cancer medicines by several international partner authorities in various countries. The ultimate aim is to give patients faster access to innovative cancer treatments. Currently, the authorisation authorities in Australia (TGA), Brazil (ANVISA), Israel (MOH), Canada (HC), Singapore (HSA), Switzerland (Swissmedic), and the United Kingdom (MHRA) are represented in Project Orbis.

Mode of action

Opdualag contains the known active substance nivolumab (a so-called PD-1 inhibitor) and the new active substance relatlimab (a LAG-3 inhibitor) in a fixed combination.

PD-1 (programmed cell death protein 1) is a receptor (target site) on immune cells. These immune cells form part of the body's natural defences. When the receptor is activated by a PD-L1 (PD-ligand 1) – a protein – the body's immune response is reduced.

Certain cancer cells can form a PD-L1 surface protein of this type, which then reduces the body's immune response to the cancer cells. Preventing the PD-L1 from binding to the PD-1 receptor by means of a PD-1 inhibitor such as nivolumab therefore increases the activity of the body's own defence system towards the tumour tissue.

Inhibition of LAG-3 (lymphocyte activation gene 3) by relatlimab also increases the activity of the body's defence system towards the tumour by means of a different mechanism of action.

Indication

Opdualag, containing the active substances nivolumab and relatlimab, is a prescription-only medicine.

Opdualag is available as a concentrate used to make an infusion; the 20 mL vial contains 240 mg nivolumab and 80 mg relatlimab. The recommended dosage of Opdualag (480 mg nivolumab and 160 mg relatlimab) is administered every 4 weeks as a 30-minute infusion into a vein.

Efficacy

The efficacy of Opdualag was investigated in a trial (RELATIVITY-047) with 714 male and female patients who had previously untreated metastatic or unresectable melanoma. 355 patients were given nivolumab in combination with relatlimab and 359 were given nivolumab alone (monotherapy). The concentration of PD-L1 protein formed by the tumour tissue was determined in both groups. All patients were treated with the respective therapy until their disease progressed or unacceptable undesirable effects occurred.

The efficacy of the therapy was determined by progression-free survival (PFS[1]). After 12 months no PFS event had occurred in 42% of the patients in the combination group with a PD-L1 value below 1%, compared with 25% in the nivolumab group. The median[2] PFS was 6.4 months in the group given nivolumab plus relatlimab and 2.9 months in the nivolumab group.

Median overall survival (OS)[3] had not been reached in the combination group by the time the trial was evaluated, and was 27 months in the nivolumab group.

Precautions, undesirable effects & risks

Opdualag must not be used in those who are hypersensitive to the active substances or any of the excipients.

The most commonly observed undesirable effects were fatigue (39%), musculo-skeletal pain (28%), rash (22%), pruritus (20%), and joint pain (20%).

Immune-mediated undesirable effects, such as inflammatory changes in the lungs (pneumonitis), liver (hepatitis), or heart muscle (myocarditis), can also occur after the therapy has been discontinued; patients should therefore be monitored continuously for at least 5 further months.

All precautions, risks, and other possible undesirable effects are listed in the Information for healthcare professionals.

[1] PFS: progression-free survival. Period between the start of a treatment or a clinical trial and the onset of disease progression or the death of the patient.

[2] Median: The value that lies exactly in the middle of a distribution of data is called the median or central value. Half of the data values are always smaller than the median, the other half are always greater.

[3] Overall survival (OS): Overall survival refers to the period between the start of treatment and the death of the patient.

Why the medicinal product has been authorised

The RELATIVITY-047 trial showed an improvement in PFS and OS with the combination of nivolumab and relatlimab compared to monotherapy with nivolumab alone in patients with previously untreated metastatic or unresectable melanoma whose PD-L1 expression is below 1%.

Taking all the risks and precautions into account, and based on the available data, the benefits of Opdualag outweigh the risks. Swissmedic has therefore authorised the medicinal product Opdualag, with the active substances nivolumab and relatlimab, for use in Switzerland.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Opdualag®

Healthcare professionals can answer any further questions.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Public Summary SwissPAR.

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