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Outcome of assessment on use of Opdualag in the treatment of advanced melanoma

The European Medicines Agency has finalised its assessment of an application to extend the use of Opdualag (nivolumab/relatlimab) to include the treatment of advanced melanoma (a type of skin cancer that has spread or cannot be surgically removed) with PD-L1 levels of 1% of higher. PD-L1 is a protein produced by some cancer cells. Although EMA did not recommend this use, it agreed that relevant data submitted with the application be included in the medicine's product information, so that healthcare professionals have access to up-to-date data on the effects of Opdualag in patients with advanced melanoma with low PD-L1 levels (less than 1%).

What is Opdualag and what is it used for?

Opdualag is a cancer medicine used to treat patients from 12 years of age with previously untreated advanced melanoma with PD-L1 levels below 1%.

Opdualag contains the active substances nivolumab and relatlimab and is given as an infusion (drip) into a vein.

Further information on Opdualag's current uses can be found on the Agency's website.

What change had the company applied for?

The company applied to extend the use of Opdualag to treat patients from 12 years of age with previously untreated advanced melanoma with PD-L1 levels of 1% or higher.

How does Opdualag work?

The active substances in Opdualag, nivolumab and relatlimab, are monoclonal antibodies (proteins designed to attach to specific receptors (targets)).

Nivolumab attaches to a receptor called PD-1 on cells of the immune system called T cells. Cancer cells can produce proteins (PD-L1 and PD-L2) on their surface that attach to the PD-1 receptor and switch off the activity of the T cells, preventing them from attacking the cancer. By attaching to the receptor, nivolumab prevents PD-L1 and PD-L2 from switching off the T cells, thereby increasing the ability of the T cells to kill cancer cells.

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Relatlimab attaches to and blocks another receptor known as LAG-3. LAG-3 is involved in reducing the immune response. By blocking LAG-3, relatlimab activates more T cells, thereby increasing their ability to attack and kill the cancer cells.

Using nivolumab and relatlimab together is more effective at killing the cancer cells than using them alone.

In the treatment of advanced melanoma with PD-L1 levels of 1% or higher, Opdualag is expected to work in the same way as it does in its existing indication.

What did the company present to support its application?

The initial authorisation of Opdualag was based on a main study involving 714 patients with previously untreated advanced melanoma who received either Opdualag or nivolumab used alone. The main measure of effectiveness was how long patients lived without their disease getting worse. The study also included supportive data on how long patients lived overall. At the time of the initial authorisation, the Agency concluded that the data did not show a benefit of Opdualag in people with tumour PD-L1 levels of 1% or higher.

To support the use of Opdualag in people with tumour PD-L1 levels of 1% or higher, the company provided further analyses from this main study, based on data collected after 5 years of follow up. The analyses looked at how long people lived overall, including in the subgroups of people with tumour PD-L1 levels of less than 1% and people with tumour PD-L1 levels of 1% or higher.

What were EMA’s conclusions?

EMA’s human medicines committee (CHMP) concluded that the submitted analyses were not sufficient to show a beneficial effect of Opdualag in people with tumour PD-L1 levels of 1% or higher. The analysis was only exploratory, meaning that it was not designed to address the main study question, and it could not be relied on to support the use of Opdualag in patients with tumour PD-L1 levels of 1% or higher. Therefore, also considering that Opdualag is less well tolerated than nivolumab alone, the CHMP concluded that the benefits of the medicine do not outweigh its risks in patients with advanced melanoma with PD-L1 levels of 1% or higher.

Although Opdualag will not be authorised for the treatment of advanced melanoma with PD-L1 levels of 1% or higher, the prescribing information for Opdualag will be updated to include the 5-year data on the time patients with tumour PD-L1 levels below 1% lived overall, so that healthcare professionals have access to up-to-date information on the effects of Opdualag.

Does this outcome affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials using Opdualag.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.