



# Nivolumab Plus Relatlimab (Opdualag)

## FOR WHOM IS THIS DRUG APPROVED?

Nivolumab plus relatlimab-rmbw (Opdualag) is a combination immunotherapy regimen used to treat children who are 12 years and older as well as adults who have unresectable or metastatic melanoma. The FDA approved the combination in March 2022.<sup>1</sup>

## WHAT EFFICACY DATA BACK IT UP?

The efficacy of nivolumab plus relatlimab was evaluated in the phase 2/3 RELATIVITY-047 trial (NCT03470922), which included 714 patients with previously untreated metastatic or unresectable stage III or IV melanoma. Patients were allowed to have received prior adjuvant or neoadjuvant melanoma therapy that included an anti-PD1 or anti-CTLA-4 agent, or a *BRAF* or MEK inhibitor (or both) if their last dose of therapy had

been at least 6 months before the date of recurrence. Prior interferon treatment was allowed if the last dose was at least 6 weeks prior to randomization.

Patients were randomly assigned in a 1:1 fashion: 359 patients received nivolumab (Opdivo) at a dose of 480 mg intravenously every 4 weeks and 355 patients received nivolumab-relatlimab (nivolumab 480 mg and relatlimab 160 mg) every 4 weeks. Patients were also stratified by LAG-3 and PD-1 expression, *BRAF* mutation status, and metastasis stage.<sup>2</sup>

The primary end point was progression-free survival (PFS), as determined by a blinded independent central review (BICR) using RECIST V1.1 criteria. The secondary end points were overall survival (OS) and objective response rate (ORR), as determined by BICR using RECIST V1.1. The trial met its primary

end point of improved PFS.

The median PFS was 10.1 months (95% CI; 6.4 to 15.7) with nivolumab-relatlimab as compared with 4.6 months (95% CI, 3.4 to 5.6) with nivolumab (HR, 0.75; 95 CI, 0.62-0.92; *P* = .006).<sup>2</sup>

Further, at a 12-month follow-up, the rate of PFS was 47.7% (95% CI; 41.8%-53.2%) vs 36.0% (95% CI, 30.5% to 41.6%), respectively.<sup>2</sup>

## HOW OPDUALAG WORKS

Tumors are immunosuppressive and evade detection by the immune system in various ways. Immune checkpoint inhibitors such as nivolumab-relatlimab help restimulate the immune system, particularly the T cells, via various mechanisms.<sup>1</sup>

Nivolumab is a human IgG4 monoclonal antibody that works by binding to the PD-1 receptor, stopping it from interaction with its ligands PD-L1 and PD-L2, and reducing the PD-1 pathway-mediated inhibition of the immune response, including the antitumor immune response.<sup>1</sup>

Relatlimab is a human IgG4 monoclonal antibody that is designed to bind to the LAG-3 receptor, inhibiting interaction with ligands including MHC II. This, in turn, reduces LAG-3 pathway-mediated inhibition of the immune response. Antagonism of this pathway leads to T-cell proliferation and cytokine secretion.<sup>1</sup>

The combination of nivolumab (anti-PD-1) and relatlimab-rmbw (anti-LAG-3) results in increased T-cell activation compared to the activity of either antibody alone.<sup>1</sup>

## HOW IT IS ADMINISTERED

Opdualag is administered once every 4 weeks. The infusion is for 30 minutes.<sup>1</sup>

## THE RECOMMENDED DOSE

Opdualag (nivolumab 480 mg and relatlimab 160 mg) is given every 4 weeks.<sup>1</sup>

## WHAT TO ADVISE PATIENTS ABOUT

Patients should be advised that although they may not experience adverse events (AEs) in the first infusion, it does not mean that they are not likely to occur. Some immune-related AEs (irAEs) may develop weeks or even months into treatment, so it is important to notify the patient's oncology team about any new AEs as they are likely to worsen if untreated. Some important AEs to be aware of are diarrhea, cough, shortness of breath, chest pain, and muscle weakness.<sup>1</sup>

## HOW TO SAFELY HANDLE THIS AGENT?

The injection is a sterile, preservative-free, clear-to-opalescent, colorless-to-slightly-yellow solution for intravenous use supplied in a single-dose vial containing 240 mg of nivolumab and 80 mg of relatlimab per 20 mL (12 mg and 4 mg per mL, respectively) per carton (NDC 0003-7125-11).<sup>1</sup>

The solution should be refrigerated and stored at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect it from light until time of use. Do not freeze or shake.<sup>1</sup>

## AE MANAGEMENT

Patients, caregivers, and nurses should be aware of the irAEs of nivolumab-relatlimab. These can be severe or fatal and can occur in any organ system at any time during or even after completion of treatment. If irAEs are clinically suspected, treatment may need to be held or permanently discontinued depending on the severity of the AE. There is no recommended dose reduction with nivolumab-relatlimab.<sup>1</sup>

In addition to holding administration, immunosuppressive therapy will likely need to be given. This is usually in the form of corticosteroids such as prednisone 1 to 2 mg/kg, followed by a slow steroid taper (typically 10 mg per week) to reduce the risk of a rebound irAE. If the irAE cannot be sufficiently managed with pred-

## Advice for Nurses WHO ADMINISTER THIS AGENT:

Because nivolumab-relatlimab is an immunotherapy, there is a potential for immune-related adverse events (irAEs).

The irAEs are typically inflammatory reactions that result from an overactivated immune system from these immunotherapies.

They can often present as other non-treatment-related toxicities, so it is important to rule out other etiology for these AEs. Although any organ system can be affected, the most common AEs include fatigue, rash, arthralgias, myalgias, and loose stools.

Before the initial infusion, baseline vital signs, nursing assessment, complete blood count (CBC), comprehensive metabolic panel (CMP), pregnancy level, thyroid function testing, cortisol levels, and adrenocorticotropic hormone levels must be obtained. CBC and CMP are repeated every cycle to monitor for immune-mediated hepatitis. Assessment for immune-mediated colitis should be made before the administration of each cycle.



nisone, other immunosuppressive agents may need to be given.<sup>1</sup> ●

### REFERENCES

1. Opdualag. Prescribing information. Bristol-Myers Squibb Company; 2022. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2022/761234s0001bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761234s0001bl.pdf)
2. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and nivolumab versus nivolumab in untreated advanced