Opdivo

(nivolumab)

NEW INDICATION

Drug Update
Slideshow

MPR

Introduction

- **Brand name:** Opdivo
- **Generic name:** Nivolumab
- **Pharmacological class:** Human programmed death receptor-1 (PD-1)-blocking antibody
- **Strength and Formulation:** 10mg/mL; per vial; solution for IV infusion after dilution; preservative-free; contains mannitol
- **Manufacturer:** Bristol-Myers Squibb
- **How supplied:** Single-use vials (4mL, 10mL)—1
- **Legal Classification:** Rx

OPDIVO


Opdivo
(nivolumab)
injection
100 mg/10 mL
(10 mg/mL)
Opdivo
(nivolumab)
injection
40 mg/4 mL
(10 mg/mL)
Opdivo
Opdivo

New Indication

- Recurrent or metastatic **squamous cell carcinoma of the head and neck (SCCHN)** with disease progression on or after platinum-based therapy

Other Indications

- Advanced renal cell carcinoma (RCC) in patients who have received prior anti-angiogenic therapy
- Classical Hodgkin lymphoma (cHL) that relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin
- As a single agent for patients with BRAF V600 wild-type or BRAF V600 mutation (+) unresectable or metastatic melanoma
- In combination with ipilimumab for unresectable or metastatic melanoma
- Metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy

Dosage & Administration

Head and neck cancer:

- Give as IV infusion over 60mins
- 3mg/kg every 2 weeks until disease progression or unacceptable toxicity
- Dose modifications: see full labeling

Considerations for Special Populations

- **Pregnancy:** Not recommended (especially 2nd and 3rd trimesters)
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Geriatric:** No overall differences in safety or efficacy
- **Hepatic impairment:** Moderate or severe: not studied
- **Renal impairment:** No adjustment necessary

Warnings/Precautions

- See full labeling

- **Monitor** for any immune-mediated adverse reactions; permanently discontinue or withhold, and give corticosteroids (at 1–2mg/kg/day prednisone equivalents) based on severity of event

Warnings/Precautions

- **Permanently discontinue** for any life-threatening (Grade 4) adverse reaction, Grade 3 or 4 pneumonitis, Grade 3/4 recurrent colitis (with ipilimumab), Grade 4 or recurrent colitis (as single agent), AST/ALT >5XULN or total bilirubin >3XULN, SCr >6XULN, Grade 4 hypophysitis, Grade 3 or 4 adrenal insufficiency, Grade 4 hyperglycemia, Grade 4 rash (or confirmed SJS/TEN), immune-mediated encephalitis, recurring Grade 3 adverse reactions, requirement for ≥10mg/day prednisone (or equivalent) for >12 weeks, or persistent Grade 2 or 3 adverse reactions lasting ≥12 weeks

Warnings/Precautions

- Grade 2 pneumonitis, Grade 2 or 3 (as single agent) colitis, AST/ALT >3–5XULN or total bilirubin >1.5–3XULN, SCr >1.5–6XULN, Grade 2 or 3 hypophysitis, Grade 2 adrenal insufficiency, Grade 3 hyperglycemia, Grade 3 rash (or suspected SJS/TEN), new onset moderate-to-severe neurologic symptoms, other Grade 3 adverse reactions (1st occurrence); **withhold** dose, give corticosteroids, and resume when return to Grade 0 or 1

Warnings/Precautions

- **Interrupt** or **decrease** infusion rate if mild or moderate infusion reactions occur; discontinue if severe or life-threatening
- **Monitor** for abnormal liver tests, elevated serum creatinine, hyperglycemia, and thyroid function prior to and during treatment; give replacement therapy for hypothyroidism
- **Monitor** for transplant-related complications (eg, hyperacute or Grade 3/4 acute GVHD, steroid-requiring febrile syndrome, hepatic veno-occlusive disease) and treat promptly

Warnings/Precautions

- Embryo-fetal toxicity
- Females of reproductive potential should use **effective contraception** during therapy and for ≥5 months after final dose

Adverse Reactions

- Fatigue
- Rash
- Musculoskeletal pain
- Pruritus
- Diarrhea
- Nausea
- Asthenia
- Cough
- Dyspnea
- Immune-mediated reactions (may be fatal)

Mechanism of Action

- Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response

Clinical Trials

Head and neck cancer:

- Trial 9 was a randomized, active-controlled, open-label study enrolling patients with metastatic or recurrent SCCHN with disease progression during or within 6 months of receiving platinum-based therapy in either the adjuvant, neo-adjuvant, primary or metastatic setting

Clinical Trials

- Patients were randomized to receive Opdivo administered IV at 3mg/kg every 2 weeks (n=240) or investigator's choice (n=121) of:
  - Cetuximab 400mg/m^2 loading dose IV followed by 250mg/m^2 weekly
  - Methotrexate 40–60mg/m^2 IV weekly, or
  - Docetaxel 30–40mg/m^2 IV weekly
- First tumor assessments were conducted 9 weeks after randomized and continued every 6 weeks thereafter

Clinical Trials

- The **major efficacy outcome** measure was overall survival (OS); progression-free survival (PFS) and objective response rate (ORR) were additional outcome measures
- The trial showed a statistically significant improvement in OS for patients randomized to Opdivo vs. investigator's choice at a pre-specified interim analysis
  - **Opdivo:** 7.5 months (95% CI: 5.5, 9.1)
  - **Investigator's choice:** 5.1 months (95% CI: 4.0, 6.0)
  - Hazard ratio: 0.70 (95% CI: 0.53, 0.92); *P*=0.0101

Clinical Trials

- There were no statistically significant differences between the two arms for PFS or ORR:
  - **PFS:** HR 0.89 (95% CI: 0.70, 1.13)
  - **ORR:**
    - Opdivo 13.3% (95% CI: 9.3, 18.3)
    - Investigator's choice 5.8% (95% CI: 2.4, 11.6)

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/opdivo/drug/34414/#headandneckcancer