BRING THE BENEFIT OF OPDIVO® TO MORE PATIENTS[1]

OPDIVO® (nivolumab)

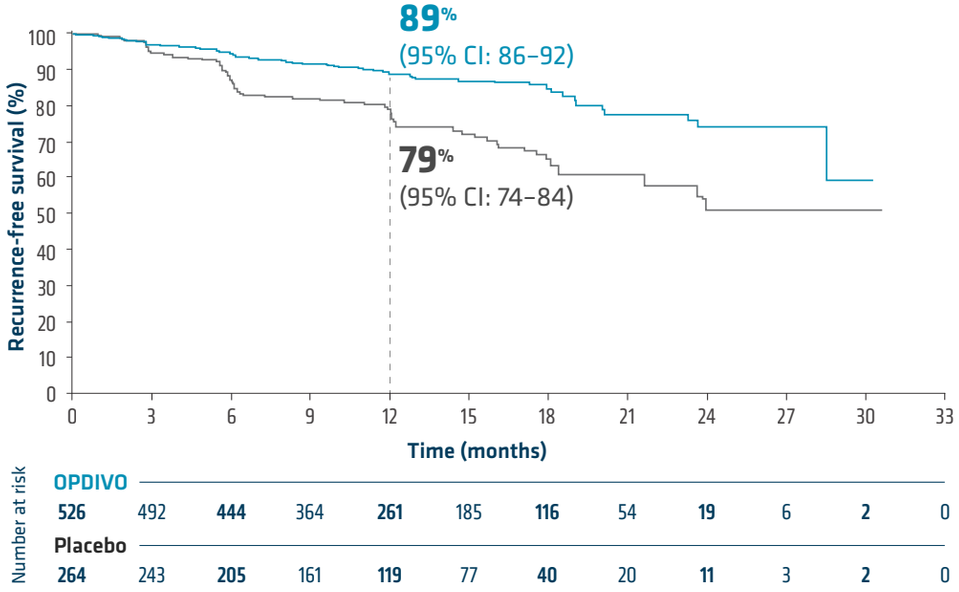
INJECTION FOR INTRAVENOUS USE 10 mg/mL

APPROVED for patients with completely resected Stage IIB/C melanoma[1]

OPDIVO® (nivolumab) is indicated for the adjuvant treatment of adult and pediatric patients 12 years and older with completely resected Stage IIB or Stage IIC melanoma.[1]

Nivolumab is a **NCCN CATEGORY 1 RECOMMENDED ADJUVANT TREATMENT OPTION** for completely resected pathological Stage IIB/C cutaneous melanoma in the **NCCN Clinical Practice Guidelines** in Oncology (NCCN Guidelines®)[2]

OPDIVO reduced the risk of recurrence* or death by 58% compared to placebo[1,3]



Median RFS, mos[1]
OPDIVO: NR (95% CI: 28.5–NR)
Placebo: NR (95% CI: 21.6–NR)
HR=0.42 (95% CI: 0.30–0.59); *P*<0.0001

Secondary Endpoint—DMFS

A HR of 0.47 was observed for DMFS for OPDIVO vs placebo[3]

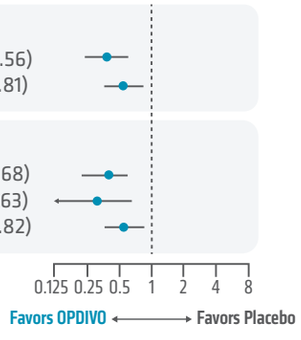
- HR vs placebo (95% CI): 0.47 (0.30–0.72)
- Median DMFS, mos (95% CI): NR (28.5–NA) with OPDIVO (n=526) vs NR with placebo (n=264)
- DMFS was not assessed for statistical significance

*Recurrence includes new primary melanoma.[1]
RFS is defined as the time between the date of randomization and the date of first recurrence (local, regional, or distant metastasis), new primary melanoma, or death, from any cause, whichever occurred first and as assessed by the investigator.[1] DMFS is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurred first.[4]

PLEASE SEE FULL STUDY DESIGN ON PAGE 3

Extended RFS rates observed regardless of disease stage or T category with OPDIVO[3†]

	OPDIVO		Placebo		
Subgroup	**Events/Patients n (N)**	**12-mo RFS rate % (95% CI)**	**Events/Patients n (N)**	**12-mo RFS rate % (95% CI)**	**Unstratified HR (95% CI)**
Disease stage					
IIB	26 (316)	92.6 (88.6–95.2)	36 (163)	84.1 (76.8–89.3)	0.34 (0.20–0.56)
IIC	40 (210)	83.8 (77.5–88.4)	33 (101)	72.0 (61.6–80.0)	0.51 (0.32–0.81)
T category					
T3b	16 (204)	92.6 (87.2–95.7)	22 (104)	83.4 (73.8–89.7)	0.36 (0.19–0.68)
T4a	10 (112)	92.6 (85.1–96.4)	14 (58)	85.2 (70.7–92.8)	0.27 (0.12–0.63)
T4b	40 (210)	83.8 (77.5–88.4)	33 (102)	72.3 (61.9–80.2)	0.52 (0.33–0.82)



These analyses were exploratory and not powered.
†vs placebo.
CI=confidence interval; DMFS=distant metastasis-free survival; HR=hazard ratio; mos=months; N=number; NA=not available; NCCN=National Comprehensive Cancer Network; NR=not reached; RFS=recurrence-free survival.

SUMMARY OF WARNINGS AND PRECAUTIONS

OPDIVO is associated with the following Warnings and Precautions: severe and fatal immune-mediated adverse reactions including pneumonitis, colitis, hepatitis and hepatotoxicity, endocrinopathies, nephritis with renal dysfunction, dermatologic adverse reactions, other immune-mediated adverse reactions; infusion-related reactions; complications of allogeneic hematopoietic stem cell transplantation (HSCT); embryo-fetal toxicity; and increased mortality in patients with multiple myeloma when OPDIVO is added to a thalidomide analogue and dexamethasone, which is not recommended outside of controlled clinical trials.

Please see additional Important Safety Information for OPDIVO on pages 3 and 4 and U.S. Full Prescribing Information for OPDIVO.

A familiar safety profile was observed for OPDIVO® (nivolumab)1*

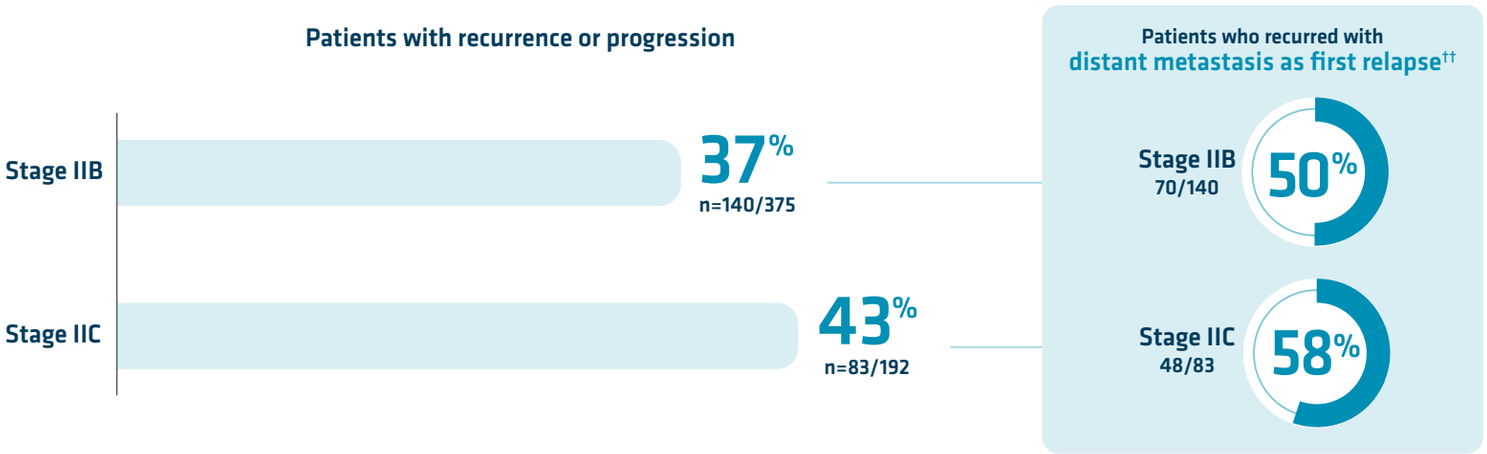
ADVERSE REACTIONS OCCURRING IN ≥10% OF PATIENTS TREATED WITH OPDIVO

Adverse events (%)	OPDIVO (n=524)		Placebo (n=264)	
	All grades (%)	Grades 3–4 (%)	All grades (%)	Grades 3–4 (%)
General				
Fatigue†	36	0.4	34	0.4
Musculoskeletal and connective tissue				
Musculoskeletal pain‡	30	0.4	26	0.4
Skin and subcutaneous tissue				
Rash§	28	1.1	15	0.4
Pruritus	20	0.2	11	0
Gastrointestinal				
Diarrhea‖	23	1.3	16	0
Nausea	14	0	11	0
Endocrine				
Hypothyroidism¶	14	0	2.3	0
Nervous system				
Headache#	12	0.2	14	0.8

*As compared to safety profile of CM-238 trial. Rates, severity, and specific reactions included under each type of adverse reaction vary across both trials. Please note the clinical trials were conducted under varying conditions, including different trial designs, patient populations, and dosing.[1] †Includes asthenia. ‡Includes arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal stiffness, myalgia, neck pain, non-cardiac chest pain, spinal pain, pain in extremity. §Includes dermatitis, dermatitis acneiform, dyshidrotic eczema, eczema, eczema asteatotic, eyelid rash, genital rash, pemphigoid, penile rash, rash erythematous, rash follicular, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, skin exfoliation, toxic skin eruption. ‖Includes autoimmune colitis, colitis, diarrhea, enteritis, enterocolitis. ¶Includes autoimmune hypothyroidism, blood thyroid stimulating hormone increased. #Includes cluster headache, migraine.

Following surgery, Stage IIB/C melanoma patients may be at a high risk of recurrence[5]

REAL-WORLD ANALYSIS: RISK OF RECURRENCE BY PATHOLOGICAL STAGE**



**Based on a retrospective analysis of 567 adult patients with Stage IIB or IIC cutaneous melanoma that was completely resected within the 10-year period from Jan 2008-Dec 2017 within the US Oncology Network database. Patients were required to have Stage IIB or IIC melanoma as evidenced by a negative sentinel lymph node biopsy at the first assessment within 12 weeks after surgical resection. Median follow-up was 41.5 months in Stage IIB and 33.4 months in Stage IIC cohorts. 14.1% (80/567) of patients in the study received any adjuvant treatment for Stage IIB or IIC melanoma; of those who received any adjuvant treatment, 96.3% (77/80) received adjuvant IFN-alfa.[5] ††Where the first physician-documented recurrence event was distant metastasis.[5] AE=adverse events; IFN=interferon.

OPDIVO significantly reduced the risk of recurrence in completely resected Stage IIB/C patients[1]—consider treatment earlier

CheckMate 76K evaluated RFS with OPDIVO q4w as adjuvant treatment for patients with completely resected Stage IIB/C melanoma[1,3]

PHASE 3, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL[1,3,4]

Eligibility criteria
- ≥12 years old
- Treatment-naïve
- ECOG PS of 0 or 1
- Completely resected Stage IIB/C melanoma with standard wide local excision
- Negative sentinel lymph node biopsy

Stratification
T category (T3b, T4a, T4b)

Follow-up time
- Minimum follow-up time was 7.8 months
- Median follow-up time:
  – OPDIVO: 15.8 months
  – Placebo: 15.9 months

*See Full Prescribing Information for recommended dosing information.
ECOG PS=Eastern Cooperative Oncology Group Performance Status; IV=intravenous; OS=overall survival; PFS2=progression-free survival through next-line therapy; q4w=every 4 weeks; R=randomization.

IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions listed herein may not include all possible severe and fatal immune-mediated adverse reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. While immune-mediated adverse reactions usually manifest during treatment, they can also occur after discontinuation of OPDIVO. Early identification and management are essential to ensure safe use of OPDIVO. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment with OPDIVO. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue OPDIVO depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if OPDIVO interruption or discontinuation is required, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

OPDIVO can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients receiving OPDIVO monotherapy, immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients, including Grade 4 (<0.1%), Grade 3 (0.9%), and Grade 2 (2.1%).

Immune-Mediated Colitis

OPDIVO can cause immune-mediated colitis. A common symptom included in the definition of colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients, including Grade 3 (1.7%) and Grade 2 (1%).

Immune-Mediated Hepatitis and Hepatotoxicity

OPDIVO can cause immune-mediated hepatitis. In patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients, including Grade 4 (0.2%), Grade 3 (1.3%), and Grade 2 (0.4%).

Immune-Mediated Endocrinopathies

OPDIVO can cause primary or secondary adrenal insufficiency, immune-mediated hypophysitis, immune-mediated thyroid disorders, and Type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Withhold OPDIVO depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism; initiate hormone replacement as clinically indicated. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism; initiate hormone replacement or medical management as clinically indicated. Monitor patients for hyperglycemia or other signs and symptoms of diabetes; initiate treatment with insulin as clinically indicated.

In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994), including Grade 3 (0.4%) and Grade 2 (0.6%).

In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients, including Grade 3 (0.2%) and Grade 2 (0.3%).

In patients receiving OPDIVO monotherapy, thyroiditis occurred in 0.6% (12/1994) of patients, including Grade 2 (0.2%).

In patients receiving OPDIVO monotherapy, hyperthyroidism occurred in 2.7% (54/1994) of patients, including Grade 3 (<0.1%) and Grade 2 (1.2%).

In patients receiving OPDIVO monotherapy, hypothyroidism occurred in 8% (163/1994) of patients, including Grade 3 (0.2%) and Grade 2 (4.8%).

In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients, including Grade 3 (0.4%) and Grade 2 (0.3%), and 2 cases of diabetic ketoacidosis.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

Immune-Mediated Nephritis with Renal Dysfunction

OPDIVO can cause immune-mediated nephritis. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients, including Grade 4 (<0.1%), Grade 3 (0.5%), and Grade 2 (0.6%).

Immune-Mediated Dermatologic Adverse Reactions

OPDIVO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes.

Withhold or permanently discontinue OPDIVO depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients, including Grade 3 (1.1%) and Grade 2 (2.2%).

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received OPDIVO monotherapy or were reported with the use of other PD- 1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions: *cardiac/vascular*: myocarditis, pericarditis, vasculitis; *nervous system*: meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy; *ocular*: uveitis, iritis, and other ocular inflammatory toxicities can occur; *gastrointestinal*: pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis; *musculoskeletal and connective tissue*: myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica; *endocrine*: hypoparathyroidism; *other (hematologic/immune)*: hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis (HLH), systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection, other transplant (including corneal graft) rejection.

Some ocular IMAR cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, which has been observed in patients receiving OPDIVO, as this may require treatment with systemic corticosteroids to reduce the risk of permanent vision loss.

Infusion-Related Reactions

OPDIVO can cause severe infusion-related reactions. Discontinue OPDIVO in patients with severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild (Grade 1) or moderate (Grade 2) infusion-related reactions. In patients receiving OPDIVO monotherapy as a 60-minute infusion, infusion-related reactions occurred in 6.4% (127/1994) of patients. In a separate trial in which patients received OPDIVO monotherapy as a 60-minute infusion or a 30-minute infusion, infusion-related reactions occurred in 2.2% (8/368) and 2.7% (10/369) of patients, respectively. Additionally, 0.5% (2/368) and 1.4% (5/369) of patients, respectively, experienced adverse reactions within 48 hours of infusion that led to dose delay, permanent discontinuation or withholding of OPDIVO.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with OPDIVO. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between OPDIVO and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with OPDIVO prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal studies, OPDIVO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO and for at least 5 months after the last dose.

Increased Mortality in Patients with Multiple Myeloma when OPDIVO is Added to a Thalidomide Analogue and Dexamethasone

In randomized clinical trials in patients with multiple myeloma, the addition of OPDIVO to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

Lactation

There are no data on the presence of OPDIVO in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 5 months after the last dose.

Serious Adverse Reactions

In Checkmate 76K, serious adverse reactions occurred in 18% of patients receiving OPDIVO (n=524). Adverse reactions which resulted in permanent discontinuation of OPDIVO in >1% of patients included arthralgia (1.7%), rash (1.7%), and diarrhea (1.1%). A fatal adverse reaction occurred in 1 (0.2%) patient (heart failure and acute kidney injury). The most frequent Grade 3-4 lab abnormalities reported in ≥1% of OPDIVO-treated patients were increased lipase (2.9%), increased AST (2.2%), increased ALT (2.1%), lymphopenia (1.1%), and decreased potassium (1.0%).

Common Adverse Reactions

In Checkmate 76K, the most common adverse reactions (≥20%) reported with OPDIVO (n=524) were fatigue (36%), musculoskeletal pain (30%), rash (28%), diarrhea (23%) and pruritus (20%).

References: 1. OPDIVO [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed February 12, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Long GV, Del Vecchio M, Weber J, et al. Adjuvant therapy with nivolumab versus placebo in patients with resected stage IIB/C melanoma (CheckMate 76K). Presented at: Society for Melanoma Research 2022 International Congress; October 17-20, 2022; Edinburgh, Scotland. **4.** Effectiveness study of nivolumab compared to placebo in prevention of recurrent melanoma after complete resection of stage IIB/C melanoma (CheckMate76K). ClinicalTrials.gov identifier: NCT04099251. https://classic.clinicaltrials.gov/ct2/show/NCT04099251. Updated July 27, 2023. Accessed August 10, 2023. **5.** Samlowski W, Silver MA, Hohlbauch A, et al. Real-world clinical outcomes of patients with stage IIB or IIC cutaneous melanoma treated at US community oncology clinics. *Future Oncol*. 2022 Oct;18(33):3755-3767.

Please see U.S. Full Prescribing Information for OPDIVO.

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