A chance to change the future for high-risk patients with urothelial carcinoma (UC)[1-4]

In the adjuvant treatment of patients with UC at high risk of recurrence after radical resection,

OPDIVO® (nivolumab) is now the ONLY FDA-approved option

for patients, regardless of prior neoadjuvant chemotherapy, nodal involvement, or PD-L1 status[1]

Checkmate 274 study information[1,2,5]

Checkmate 274 was a phase 3, randomized, double-blind, multicenter study of adjuvant OPDIVO 240 mg IV q2w* vs placebo IV q2w in patients with UC† at high risk of recurrence after radical resection (OPDIVO: n=353; placebo: n=356). Key inclusion criteria were patients with UC at high risk of recurrence after radical resection: ypT2–ypT4a‡ or ypN+‡ with prior neoadjuvant cisplatin-based chemotherapy and pT3–pT4a‡ or pN+‡ without prior neoadjuvant cisplatin-based chemotherapy and not eligible for or refused adjuvant cisplatin-based chemotherapy; radical resection within the last 120 days; disease-free status within 4 weeks before randomization; ECOG PS 0–1 (PS 2 if no neoadjuvant cisplatin-based chemotherapy and ineligible for adjuvant cisplatin-based chemotherapy). Patients were stratified by PD-L1 status§ (≥1% vs <1% or indeterminate), prior neoadjuvant cisplatin-based chemotherapy (yes vs no), and nodal status (N+ vs N0/X with <10 nodes removed vs N0 with ≥10 nodes removed). Patients were treated until recurrence or unacceptable toxicity for a maximum of 1 year. The primary endpoints were DFS (investigator assessed) in all randomized patients and in patients with PD-L1 ≥1%. A key secondary endpoint was OS.[1,2,5‖]

- This trial excluded patients with any condition requiring systemic treatment with immunosuppressants (eg, glucocorticoids) within 2 weeks of treatment[6]
- DFS was defined as time to first recurrence (local urothelial tract, local non-urothelial tract, or distant metastasis), or death[1]
- Minimum follow-up time in all randomized patients was 5.9 months. Median follow-up time in all randomized patients was 20.9 months for OPDIVO and 19.5 months for placebo[2]

*Approved dosing for OPDIVO is 240 mg IV q2w or 480 mg IV q4w.[1]
†Urothelial carcinoma originating in the bladder or upper urinary tract (renal pelvis or ureter).[1]
‡AJCC tumor stage.[7]
§Using the PD-L1 IHC 28-8 pharmDx assay.[1]
‖OS data are immature at the time of the planned interim analysis.[1]

AJCC=American Joint Committee on Cancer; DFS=disease-free survival; ECOG=Eastern Cooperative Oncology Group; IHC=immunohistochemistry; IV=intravenous; OS=overall survival; PD-L1=programmed death ligand 1; PS=performance status; q2w=every 2 weeks; q4w=every 4 weeks.

INDICATION

OPDIVO, as a single agent, is indicated for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.

SELECT 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.

Please see additional Important Safety Information for OPDIVO throughout and US Full Prescribing Information for OPDIVO.

OPDIVO® (nivolumab)
INJECTION FOR INTRAVENOUS USE 10 mg/mL

In a retrospective observational cohort study of patients 65 years and older with UC at high risk† of recurrence after radical resection[8]*

median disease-free survival‡ was just over 1 year§ (13.5 months)[8]
Patients who received neoadjuvant chemotherapy were also included[8]

Patients with UC need approved adjuvant options that help extend disease-free survival[8,9]

*This study included 665 patients from the SEER-Medicare database who had UC of the bladder or upper tract at a high risk of recurrence after radical resection.[8] †Prior neoadjuvant chemotherapy: AJCC stage T2–T4a or N+ and M0 for bladder site and AJCC stage T2–T4 or N+ and M0 for other sites; no neoadjuvant chemotherapy: AJCC stage T3–T4a or N+ and M0 for bladder site and AJCC stage T3–T4 or N+ and M0 for other sites.[8] ‡DFS was defined as the first occurrence of surgery, radiotherapy, ≥1 administration of systemic chemotherapy, or palliative TURBT after 120 days of primary surgical resection. Those who received adjuvant treatment within 120 days of radical resection were excluded from the study.[8] §mDFS was 13.5 months (95% CI: 11.3–16.8).[8]

OPDIVO® (nivolumab) is now the ONLY FDA-approved option for patients with UC at high risk of recurrence after radical resection, regardless of prior neoadjuvant chemotherapy, nodal involvement, or PD-L1 status[1]

AJCC=American Joint Committee on Cancer; CI=confidence interval; DFS=disease-free survival; mDFS=median DFS; SEER=National Cancer Institute's Surveillance, Epidemiology, and End Results; TURBT=transurethral resection of bladder tumor; UC=urothelial carcinoma.

SELECT IMPORTANT SAFETY INFORMATION

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

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%).

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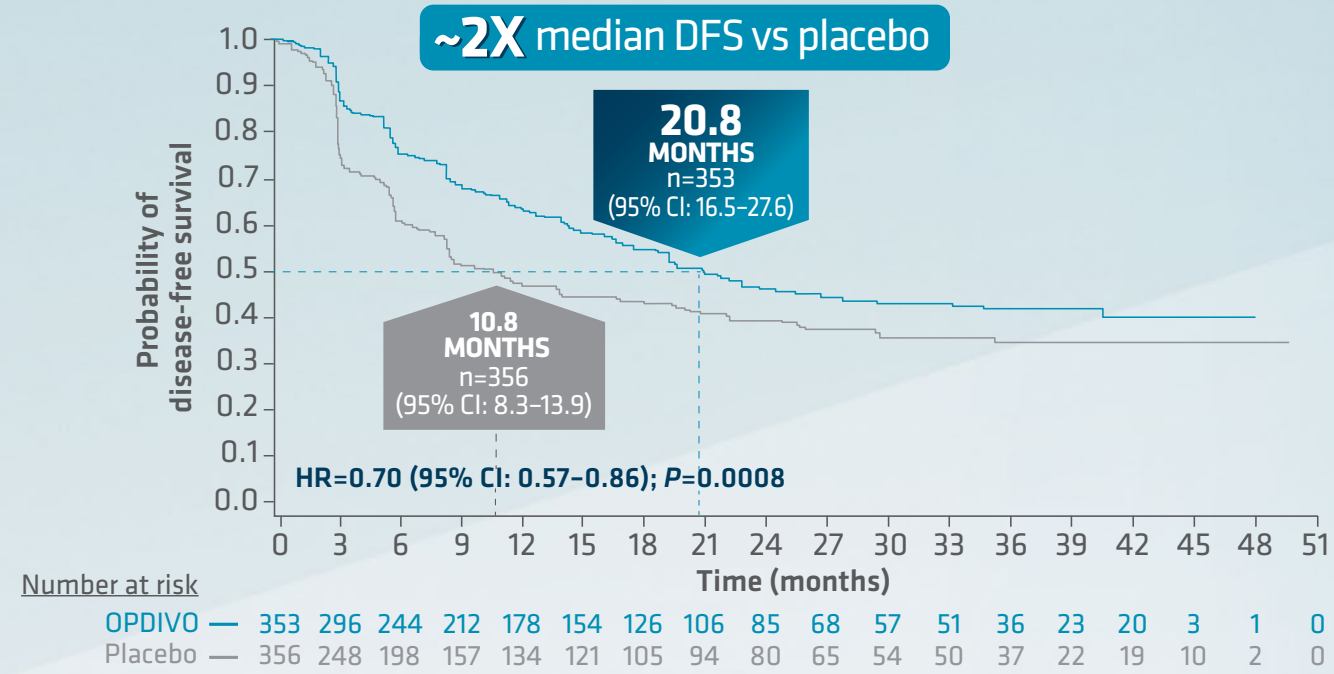
In the adjuvant treatment of patients with UC at high risk of recurrence after radical resection

Nearly double median DFS with OPDIVO® (nivolumab)[1,2*]

Disease-free survival in all randomized patients[1,2]



Minimum follow-up time of 5.9 months. Median follow-up time of 20.9 months for OPDIVO and 19.5 months for placebo.[2]

*Vs placebo.[1,2]

mDFS in patients with PD-L1 ≥1% (minimum follow-up time of 6.3 months; median follow-up time of 22.1 months for OPDIVO and 18.7 months for placebo)[1,10]

- OPDIVO (n=140): NR (95% CI: 21.2–NE)[1]
- Placebo (n=142): 8.4 months (95% CI: 5.6–21.2)[1]
- HR=0.55 (95% CI: 0.39–0.77); *P*=0.0005[1]

CI=confidence interval; DFS=disease-free survival; HR=hazard ratio; mDFS=median DFS; NE=not estimable; NR=not reached; PD-L1=programmed death ligand 1; UC=urothelial carcinoma.

SELECT IMPORTANT SAFETY INFORMATION

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

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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OPDIVO® (nivolumab)
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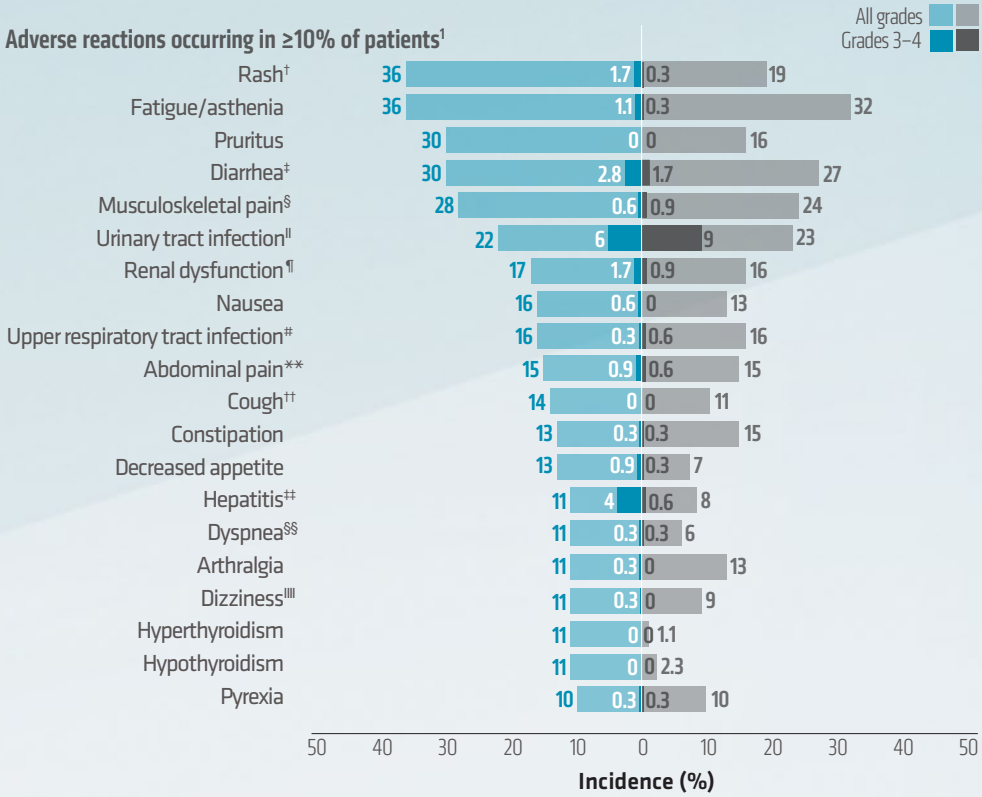
In the adjuvant treatment of patients with UC at high risk of recurrence after radical resection

What are your safety expectations for OPDIVO® (nivolumab) in the adjuvant setting?

Grade ≥3 AEs occurred in 42.7% of patients receiving OPDIVO and in 36.8% of patients receiving placebo[2]

	OPDIVO (n=351)		Placebo (n=348)	
Events, %	Any grade (%)	Grade ≥3 (%)*	Any grade (%)	Grade ≥3 (%)
Any-cause AEs[2]	98.9	42.7	95.4	36.8

Adverse reactions occurring in ≥10% of patients[1]



Toxicity was graded per NCI CTCAE v4.[1]

*Fatal adverse reactions occurred in 1% of patients; these included events of pneumonitis (0.6%).[1]

†Includes acne, blister, dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis contact, eczema, eczema asteatotic, eczema nummular, erythema, erythema multiforme, lichen sclerosus, lichenoid keratosis, pemphigoid, photosensitivity reaction, pigmentation disorder, psoriasis, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rosacea, skin exfoliation, skin lesion, skin reaction, toxic skin eruption, and urticaria.[1]

‡Includes colitis, colitis microscopic, diarrhea, duodenitis, enteritis, and immune-mediated enterocolitis.[1]

§Includes musculoskeletal pain, back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, myalgia, neck pain, pain in extremity, and spinal pain.[1]

‖Includes cystitis, escherichia urinary tract infection, pyelonephritis, pyelonephritis acute, pyelonephritis chronic, urethritis, urinary tract infection, urinary tract infection bacterial, urinary tract infection staphylococcal, and urosepsis.[1]

¶Includes acute kidney injury, autoimmune nephritis, blood creatinine increased, glomerular filtration rate decreased, immune-mediated nephritis, nephritis, renal failure, and renal impairment.[1]

#Includes upper respiratory tract infection, nasopharyngitis, pharyngitis, and rhinitis.[1]

**Includes abdominal pain, abdominal discomfort, abdominal tenderness, lower and upper abdominal pain.[1]

††Includes cough, productive cough, and upper-airway cough syndrome.[1]

‡‡Includes aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, cholangitis, drug-induced liver injury, hepatic failure, hepatic function abnormal, hepatitis, hepatocellular injury, hyperbilirubinemia, gamma-glutamyltransferase increased, liver injury, and transaminases increased.[1]

§§Includes dyspnea and exertional dyspnea.[1]

‖‖Includes dizziness, postural dizziness, and vertigo.[1]

- OPDIVO was discontinued for adverse reactions in 18% of patients. OPDIVO was delayed for adverse reactions in 33.3% of patients[1,11]
- Placebo was discontinued for adverse reactions in 6% of patients. Placebo was delayed for adverse reactions in 25.9% of patients[11]
- Serious adverse reactions occurred in 30% of OPDIVO patients[1]
- The most frequent serious adverse reaction reported in ≥2% of patients was urinary tract infection. Fatal adverse reactions occurred in 1% of patients; these included events of pneumonitis (0.6%)[1]
- The most common adverse reactions (reported in ≥20% of patients) were rash, fatigue, diarrhea, pruritus, musculoskeletal pain, and urinary tract infection[1]

AE=adverse event; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; UC=urothelial carcinoma.

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OPDIVO® (nivolumab)
INJECTION FOR INTRAVENOUS USE 10 mg/mL

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® (nivolumab). 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.

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.
- 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.

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OPDIVO® (nivolumab)

INJECTION FOR INTRAVENOUS USE 10 mg/mL

IMPORTANT SAFETY INFORMATION (cont'd)

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 274, serious adverse reactions occurred in 30% of patients receiving OPDIVO (n=351). The most frequent serious adverse reaction reported in ≥2% of patients receiving OPDIVO was urinary tract infection. Fatal adverse reactions occurred in 1% of patients; these included events of pneumonitis (0.6%).

Common Adverse Reactions

- In Checkmate 274, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=351) were rash (36%), fatigue (36%), diarrhea (30%), pruritus (30%), musculoskeletal pain (28%), and urinary tract infection (22%).

In the ADJUVANT treatment of patients with UC at high risk of recurrence after radical resection

Choose OPDIVO® (nivolumab) for your next patient in need of treatment in the adjuvant setting

Now, there is FINALLY an option that is FDA approved,

regardless of prior neoadjuvant chemotherapy, nodal involvement, or PD-L1 status[1]

DFS=disease-free survival; PD-L1=programmed death ligand 1; UC=urothelial carcinoma.

References: 1. OPDIVO [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. **2.** Bajorin DF, Witjes JA, Gschwend JE, et al. Adjuvant nivolumab versus placebo in muscle-invasive urothelial carcinoma. *N Engl J Med*. 2021;384(22):2102-2114. **3.** Jodon G, Fischer S, Kessler ER. Treatment of urothelial cancer in elderly patients: focus on immune checkpoint inhibitors. *Drugs Aging*. 2018;35(5):409-421. **4.** Duplisea JJ, Dinney CPN. Should chemotherapy still be used to treat all muscle invasive bladder cancer in the "era of immunotherapy"? *Expert Rev Anticancer Ther*. 2019;19(7):543-545. **5.** Bajorin DF, Witjes JA, Gschwend JE, et al. First results from the phase 3 Checkmate 274 trial of adjuvant nivolumab versus placebo in patient who underwent radical surgery for high-risk muscle-invasive urothelial carcinoma. Oral presentation at ASCO GU 2021. Abstract 391. **6.** Bajorin DF, Witjes JA, Gschwend JE, et al. Adjuvant nivolumab versus placebo in muscle-invasive urothelial carcinoma. *N Engl J Med*. 2021;384(22):2102-2114 [supplementary appendix]. **7.** American Cancer Society. Bladder cancer early detection, diagnosis, and staging. Accessed February 24, 2021. https://www.cancer.org/content/dam/CRC/PDF/Public/8559.00.pdf. **8.** Drakaki A, Pantuck A, Mhatre SK, et al. "Real-world" outcomes and prognostic indicators among patients with high-risk muscle-invasive urothelial carcinoma. *Urol Oncol*. 2021;39:76.e15-76.e22. **9.** Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol*. 2001;3(19):666-675. **10.** Data on file. NIVO 639. Princeton, NJ: Bristol-Myers Squibb Company; 2021. **11.** Data on file. NIVO 652. Princeton, NJ: Bristol-Myers Squibb Company; 2021.

Please see additional Important Safety Information for OPDIVO throughout and US Full Prescribing Information for OPDIVO.

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