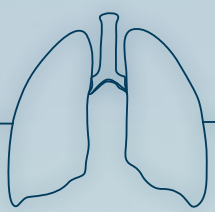


OPDIVO® (nivolumab) + CHEMO

FIRST AND ONLY NEOADJUVANT IMMUNOTHERAPY COMBINATION IN RESECTABLE NSCLC

GIVE YOUR RESECTABLE NSCLC PATIENTS A CHANCE TO START STRONG*

Neoadjuvant OPDIVO® + chemo has demonstrated the ability to significantly increase pCR and reduce the risk of progression, recurrence, or death[1,2†‡]

- 24% pCR (95% CI: 18.0–31.0) with neoadjuvant OPDIVO + chemo vs 2.2% (95% CI: 0.6–5.6) with chemo. Estimated treatment difference: 21.6% (95% CI: 15.1–28.2); *P*<0.0001[1]
- mEFS was 31.6 months (95% CI: 30.2–NR) with neoadjuvant OPDIVO + chemo vs 20.8 months (95% CI: 14.0–26.7) with chemo; HR=0.63 (95% CI: 0.45–0.87); *P*=0.0052[1]

☑ **Tumors ≥4 cm** or ☑ **Node positive (N1, N2)** | **Regardless of PD-L1 expression**

*Measured by pCR.[1] †vs chemo.[1] ‡Measured by event-free survival.[3]

CI=confidence interval; HR=hazard ratio; mEFS=median event-free survival; NR=not reached; pCR=pathological complete response; PD-L1=programmed death ligand 1.

INDICATION

OPDIVO, in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC).

IMPORTANT SAFETY INFORMATION

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.

Severe and Fatal Immune-Mediated Adverse Reactions

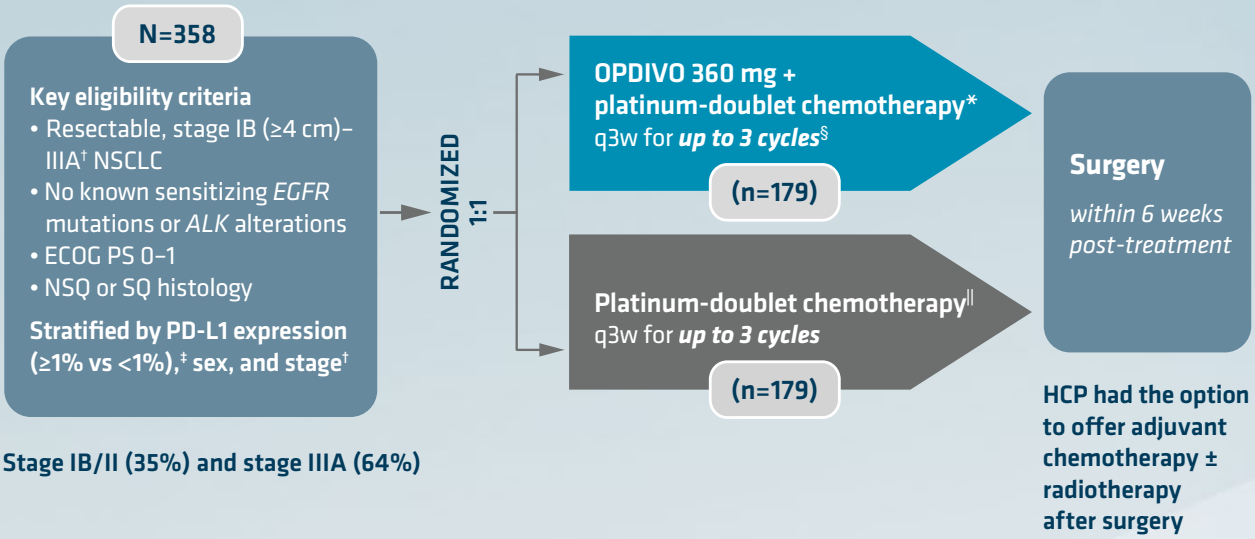
- Immune-mediated adverse reactions listed herein may not include all possible severe and fatal immune-mediated adverse reactions.
- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. While immune-mediated adverse reactions usually manifest during 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.

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

Bristol Myers Squibb™

Checkmate 816: For patients with resectable NSCLC, regardless of PD-L1 expression

Neoadjuvant OPDIVO® (nivolumab) + chemo: 3 cycles of treatment studied in stage IB–IIIA resectable NSCLC patients[1,2*]



- **83% of patients treated with neoadjuvant OPDIVO + chemo received definitive surgery and 75% with chemo[1]**
- **Primary endpoints**
  - **Pathological complete response (pCR) per BIPR:** 0% residual viable tumor in both the primary tumor (lung) and sampled lymph nodes[2¶]
  - **Event-free survival (EFS) per BICR:** Time from randomization to disease progression that precludes surgery, disease progression/recurrence after surgery, progression for patients without surgery, or death due to any cause[3]
- **Key secondary endpoint**
  - **Overall survival (OS)[1]**
- The trial excluded patients with unresectable or metastatic NSCLC, known *EGFR* mutations or *ALK* translocations, Grade 2 or greater peripheral neuropathy, active autoimmune disease, or medical conditions requiring systemic immunosuppression[1]
- Within the ITT population, 50% had tumors with PD-L1 expression ≥1%; 51% had tumors with squamous histology and 49% had tumors with non-squamous histology[1]

*Platinum-doublet chemotherapy q3w for 3 cycles: NSQ: pemetrexed and cisplatin or paclitaxel and carboplatin; SQ: gemcitabine and cisplatin or paclitaxel and carboplatin.[2] †Per the 7th edition American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) staging criteria.[1] ‡Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); PD-L1 <1% stratification includes patients with PD-L1 expression status not evaluable and indeterminate.[2] §The approved Prescribing Information recommended dosage of OPDIVO + platinum-doublet chemo is 360 mg q3w with platinum-doublet chemo on the same day q3w for 3 cycles.[1] ‖In the platinum-doublet chemotherapy arm, 2 additional treatment regimen options included vinorelbine and cisplatin, or docetaxel and cisplatin (any histology).[1] ¶Includes those not undergoing surgery who will be considered as not achieving pCR.[2]

ALK=anaplastic lymphoma kinase; BICR=blinded independent central review; BIPR=blinded independent pathological review; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; IHC=immunohistochemistry; NSQ=non-squamous; q3w=every 3 weeks.

IMPORTANT SAFETY INFORMATION (cont'd)

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

- 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%).

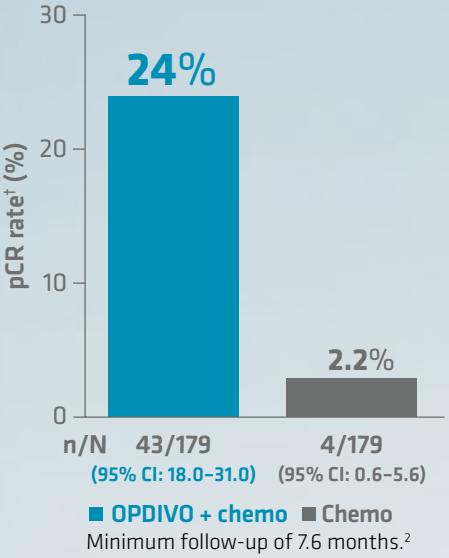
Please see additional Important Safety Information for OPDIVO throughout and US Full Prescribing Information for **OPDIVO**.

OPDIVO® (nivolumab)

Checkmate 816: For patients with resectable NSCLC, regardless of PD-L1 expression

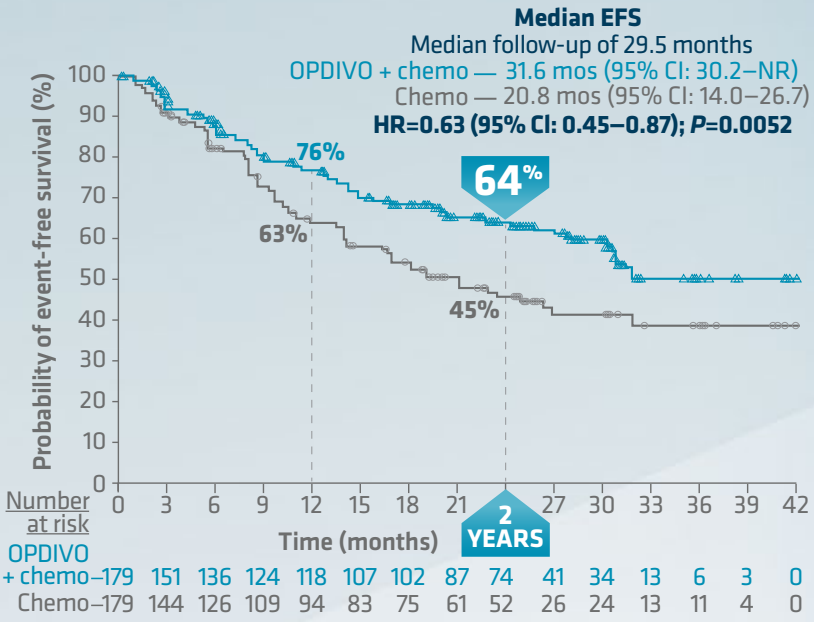
Superior pCR and EFS with neoadjuvant OPDIVO® (nivolumab) + chemo in the ITT population at the primary analysis[1,2*]

pCR ITT, primary analysis[1,2†]



Minimum follow-up of 7.6 months.[2]

EFS ITT, primary analysis[1,3‡]



- **pCR (per BIPR):** 0% residual viable tumor in both the primary tumor (lung) and sampled lymph nodes[2†]
- **EFS (per BICR):** Time from randomization to disease progression that precludes surgery, disease progression/recurrence after surgery, progression for patients without surgery, or death due to any cause[3]
- In the ITT population, the estimated treatment difference for pCR rate was 21.6% (95% CI: 15.1–28.2); *P*<0.0001[1]

pCR rate by stage and PD-L1 expression subgroups:

Limitation: Checkmate 816 was not powered to detect differences in treatment effect within individual stage or PD-L1 subgroups; therefore, this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroup.

- With a minimum follow-up of 7.6 months[2]:
  - In patients with stage I–IIB disease (n= 128) at baseline, 26% achieved pCR with OPDIVO + chemo and 5% with chemo[2,4§‖]
  - In patients with stage IIIA disease (n=228) at baseline, 23% achieved pCR with OPDIVO + chemo and 1% with chemo[2,4§‖]
  - In patients with PD-L1 <1% (n=155), 17% of patients achieved pCR with OPDIVO + chemo and 3% with chemo[2]
  - In patients with PD-L1 ≥1% (n=178), 33% of patients achieved pCR with OPDIVO + chemo and 2% with chemo[2]
- Of patients enrolled in the OPDIVO + chemo arm, 44% had tumors expressing PD-L1 <1% and 50% had tumors expressing PD-L1 ≥1%. Of patients enrolled in the chemo arm, 43% had tumors expressing PD-L1 <1% and 50% had tumors expressing PD-L1 ≥1%[2]

*vs chemo.[1] †Per BIPR. Includes those not undergoing surgery who will be considered as not achieving pCR.[2] ‡Per BICR.[3] §Baseline stage of disease by CRF; TNM 7th edition used for classification.[1] ‖Per BIPR in the ITT population.[1]

ITT=intent to treat.

IMPORTANT SAFETY INFORMATION (cont'd)

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

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%)

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

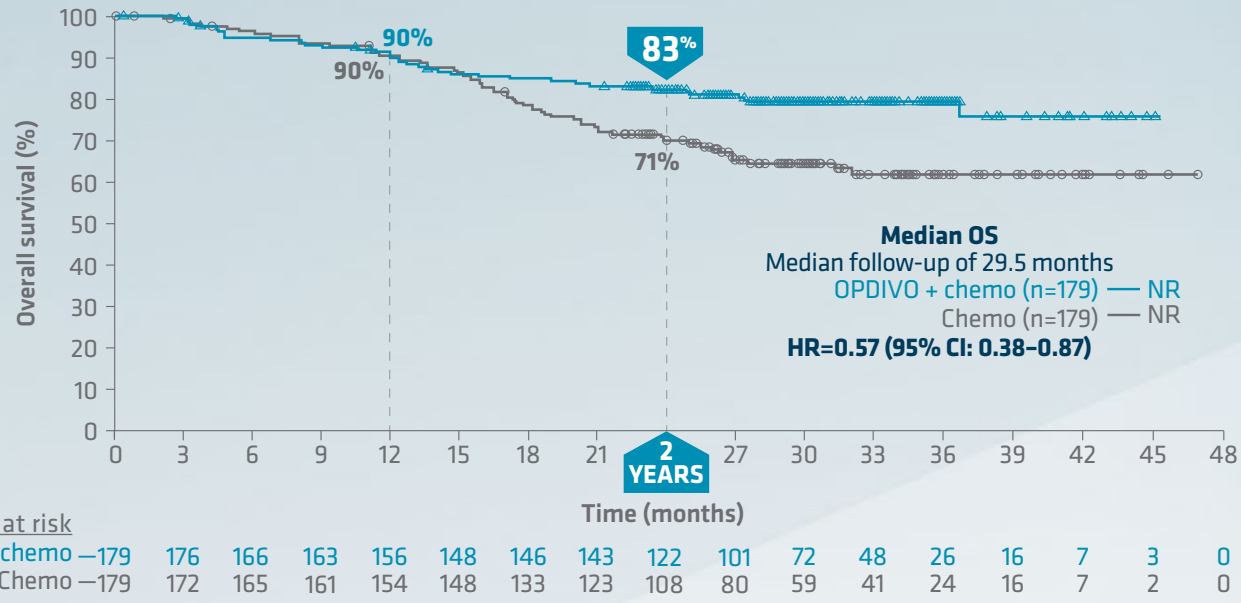
OPDIVO® (nivolumab)

Checkmate 816: For patients with resectable NSCLC, regardless of PD-L1 expression

Overall survival with neoadjuvant OPDIVO® (nivolumab) + chemo

OS ITT, pre-specified interim analysis[3]

Limitation: Results at the pre-specified interim analysis did not cross the boundary for statistical significance and should be interpreted with caution due to the immaturity of the data. OS will be monitored over time.



Number at risk

OPDIVO + chemo —179	176	166	163	156	148	146	143	122	101	72	48	26	16	7	3	0
Chemo —179	172	165	161	154	148	133	123	108	80	59	41	24	16	7	2	0

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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%).

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

OPDIVO® (nivolumab)

Checkmate 816: For patients with resectable NSCLC, regardless of PD-L1 expression

Neoadjuvant OPDIVO® (nivolumab) + chemo safety profile[1]

Adverse reactions in >10% of patients receiving OPDIVO + chemo*

Adverse reactions	OPDIVO + chemo (n=176)		Chemo (n=176)	
	All grades (%)	Grades 3–4 (%)	All grades (%)	Grades 3–4 (%)
Gastrointestinal				
Nausea	38	0.6	45	1.1
Constipation	34	0	32	1.1
Vomiting	11	1.1	13	0.6
General				
Fatigue†	26	2.3	23	1.1
Malaise	15	0.6	14	0.6
Metabolism and nutrition				
Decreased appetite	20	1.1	23	2.3
Skin and subcutaneous tissue				
Rash‡	20	2.3	7	0
Alopecia	11	0	15	0
Nervous system				
Peripheral neuropathy§	13	0	6	0

- The most common (>20%) adverse reactions were nausea (38%), constipation (34%), fatigue (26%), decreased appetite (20%), and rash (20%)[1]
- Serious adverse reactions occurred in 30% of patients[1]
  - Serious adverse reactions in >2% included pneumonia and vomiting[1]
- 10% of patients discontinued therapy due to adverse reactions[1]
- 30% of patients had at least one treatment withheld for an adverse reaction[1]

*Toxicity was graded per NCI CTCAE v4.[1] †Includes fatigue and asthenia.[1] ‡Includes rash, dermatitis, acneiform dermatitis, atopic dermatitis, bullous dermatitis, drug eruption, maculopapular rash, and pruritic rash.[1] §Includes peripheral neuropathy, dysesthesia, hypoesthesia, peripheral motor neuropathy, peripheral sensory neuropathy.[1]

NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (cont'd)

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

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

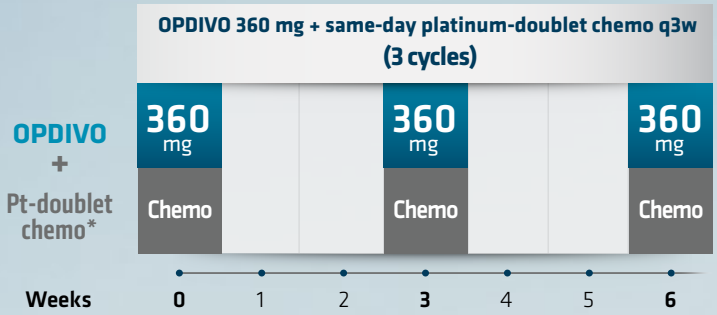
- OPDIVO can cause severe infusion-related reactions. Discontinue OPDIVO in patients with severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild (Grade 1) or moderate (Grade 2) infusion-related reactions. In patients receiving 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.

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

OPDIVO® (nivolumab)

Checkmate 816: For patients with resectable NSCLC, regardless of PD-L1 expression

OPDIVO® (nivolumab) + chemo: 3 cycles of treatment prior to surgery[1,2*]



- OPDIVO is administered as an IV infusion over 30 minutes[1]
- Refer to the respective Prescribing Information for each therapeutic agent for the recommended dosage and administration information as appropriate
- Administer OPDIVO first, followed by platinum-doublet chemotherapy on the same day[1*]
- No premedication is required with OPDIVO[1]

Treat early with OPDIVO + chemo to provide a chance for increased pCR and extended EFS[†]

☑ Tumors ≥4 cm or ☑ Node positive (N1, N2) | Regardless of PD-L1 expression

- **pCR rate:** 24% (95% CI: 18.0–31.0) with neoadjuvant OPDIVO + chemo vs 2.2% (95% CI: 0.6–5.6) with chemo. Estimated treatment difference: 21.6% (95% CI: 15.1–28.2); $P<0.0001$[1]
- **EFS:** mEFS was 31.6 months (95% CI: 30.2–NR) with neoadjuvant OPDIVO + chemo vs 20.8 months (95% CI: 14.0–26.7) with chemo; HR=0.63 (95% CI: 0.45–0.87); $P=0.0052$[1]

*Platinum-doublet chemotherapy consisted of paclitaxel 175 mg/m^2 or 200 mg/m^2 and carboplatin AUC 5 or AUC 6 (any histology); pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 (non-squamous histology); or gemcitabine 1000 mg/m^2 or 1250 mg/m^2 and cisplatin 75 mg/m^2 (squamous histology). In the platinum-doublet chemotherapy arm, two additional treatment regimen options included vinorelbine 25 mg/m^2 or 30 mg/m^2 and cisplatin 75 mg/m^2, or docetaxel 60 mg/m^2 or 75 mg/m^2 and cisplatin 75 mg/m^2 (any histology).[1] [†]vs chemo.[1]

AUC=area under the curve; IV=intravenous; Pt=platinum.

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 816, serious adverse reactions occurred in 30% of patients (n=176) who were treated with OPDIVO in combination with platinum-doublet chemotherapy. Serious adverse reactions in >2% included pneumonia and vomiting. No fatal adverse reactions occurred in patients who received OPDIVO in combination with platinum-doublet chemotherapy.

Common Adverse Reactions

- In Checkmate 816, the most common (>20%) adverse reactions in the OPDIVO plus chemotherapy arm (n=176) were nausea (38%), constipation (34%), fatigue (26%), decreased appetite (20%), and rash (20%).

Please see US Full Prescribing Information for **OPDIVO**.

References: 1. OPDIVO [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. **2.** Forde PM, Spicer J, Lu S, et al. Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB–IIIA) non-small cell lung cancer in the phase 3 CheckMate 816 trial. Oral presentation at AACR 2021. Abstract CT003. **3.** Girard N, Spicer J, Provencio M, et al. Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB–IIIA) non-small cell lung cancer: event-free survival results from the phase 3 CheckMate 816 trial. Oral presentation at AACR 2022. Abstract CT012. **4.** Spicer J, Wang C, Tanaka F, et al. Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab (nivo) + platinum-doublet chemotherapy vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer. Oral presentation at ASCO 2021. Abstract 8503.

Bristol Myers Squibb™

OPDIVO® (nivolumab)