NOW APPROVED REGARDLESS OF PD-L1 EXPRESSION[1]

OPDIVO® (nivolumab), alone or in combination,*† is the only I-O therapy to demonstrate superior survival† for gastroesophageal cancers in both the adjuvant and 1L metastatic treatment settings[1]

OPDIVO® (nivolumab)

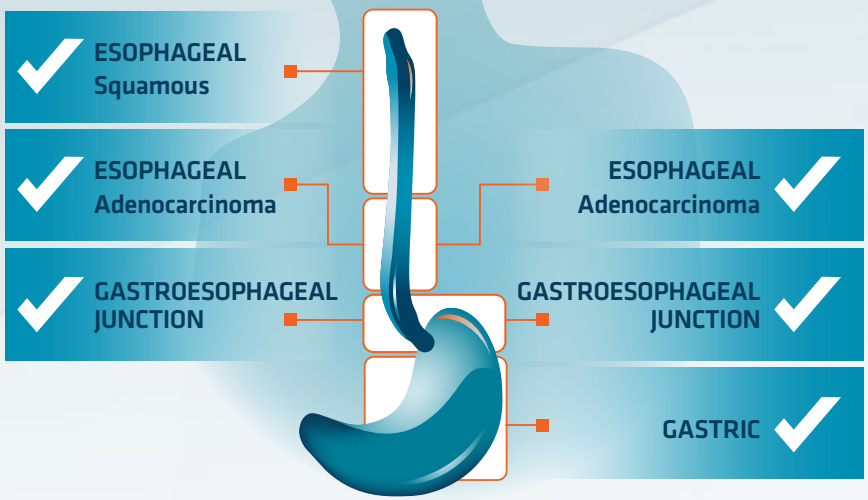
ADJUVANT

2X THE MEDIAN DFS[1]

*OPDIVO is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in patients who have received neoadjuvant chemoradiotherapy (CRT).

†**mDFS: 22.4 mos** (95% CI: 16.6–34.0) with OPDIVO vs **11.0 mos** (95% CI: 8.3–14.3) with placebo; HR=0.69 (95% CI: 0.56–0.85); *P*=0.0003.[1]

Please see page 5 for trial design and additional efficacy data for Checkmate 577.



OPDIVO® (nivolumab) + FOLFOX or CapeOX

METASTATIC

55% of patients alive at 1 year[2]

*OPDIVO, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.[1]

1-year OS rate†‡ in all comers§: 55% of patients alive with OPDIVO + FOLFOX‖ or CapeOX vs 48% with chemotherapy¶ alone.[2]

All comers§ mOS†‡: 13.8 mos (95% CI: 12.6–14.6) with OPDIVO + FOLFOX‖ or CapeOX vs **11.6 mos** (95% CI: 10.9–12.5) with chemotherapy¶ alone; HR=0.80 (95% CI: 0.71–0.90); *P*=0.0002.[2]

The 1-year OS rate analysis was exploratory and not pre-specified within the study protocol.[2]

*OPDIVO + FOLFOX or CapeOX vs FOLFOX or CapeOX alone.[1] †Based on confirmed response.[1] ‡Assessed using BICR; secondary endpoint.[1] §All comers refers to all randomized patients in Checkmate 649.[1] ‖mFOLFOX6 (leucovorin, fluorouracil, and oxaliplatin) regimen was given in Checkmate 649.[1] ¶FOLFOX (leucovorin, fluorouracil, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).[1]

Please see page 2 for trial design and additional efficacy data for Checkmate 649.

1L=first line; CI=confidence interval; DFS=disease-free survival; HR=hazard ratio; I-O=immuno-oncology; mDFS=median DFS; mo=month; OS=overall survival.

SELECT 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.

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

OPDIVO® (nivolumab)

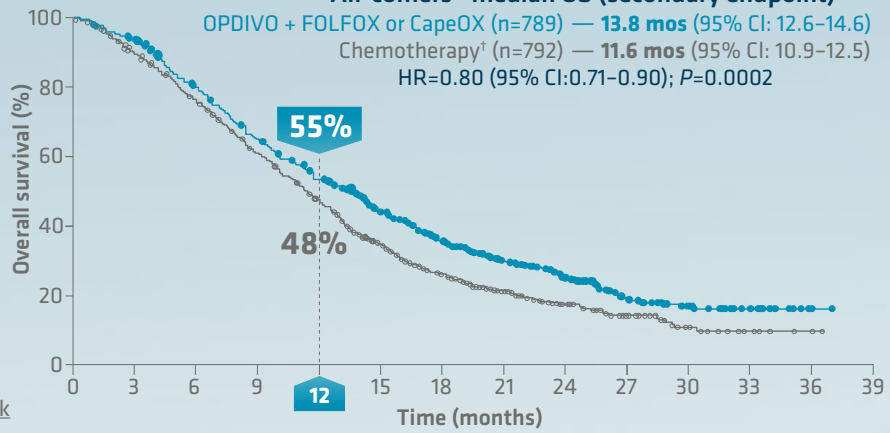
INJECTION FOR INTRAVENOUS USE 10 mg/mL

In 1L patients with metastatic GC, GEJC, and EAC

OPDIVO® (nivolumab) + FOLFOX or CapeOX: the only I-O regimen with 55% of patients alive at 1 year[1,2]

All-comers* median OS (secondary endpoint)

OPDIVO + FOLFOX or CapeOX (n=789) — **13.8 mos** (95% CI: 12.6–14.6)
Chemotherapy† (n=792) — **11.6 mos** (95% CI: 10.9–12.5)
HR=0.80 (95% CI:0.71–0.90); *P*=0.0002



Number at risk

OPDIVO + FOLFOX or CapeOX	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemotherapy†	792	697	586	469	359	239	160	94	59	35	15	7	2	0

- The 12-month OS rate analysis was exploratory and not pre-specified within the study protocol[2]

Dual primary endpoints in the PD-L1 CPS ≥5 population (n=955)[1]

- **mOS: 14.4 mos** (95% CI: 13.1–16.2) with OPDIVO + FOLFOX or CapeOX vs **11.1 mos** (95% CI: 10.0–12.1) with chemotherapy† alone; HR=0.71 (95% CI: 0.61–0.83); *P*<0.0001
- **mPFS: 7.7 mos** (95% CI: 7.0–9.2) with OPDIVO + FOLFOX or CapeOX vs **6.0 mos** (95% CI: 5.6–6.9) with chemotherapy† alone; HR=0.68 (95% CI: 0.58–0.79); *P*<0.0001

OPDIVO IS THE ONLY 1L I-O THERAPY[1,2]:

APPROVED‡ REGARDLESS OF PD-L1 EXPRESSION IN 3 GASTROESOPHAGEAL TUMOR TYPES

STUDIED IN A PHASE 3 TRIAL WITH FOLFOX AND CAPEOX§

TO OFFER Q2W AND Q3W DOSING DESIGNED TO MATCH YOUR CHEMO PREFERENCES‡§

Please see page 3 for dosage and administration

Click to view additional efficacy data: PD-L1 CPS ≥5 (primary endpoint) and PD-L1 CPS ≥1 OS K-M curves

Checkmate 649 trial design: Checkmate 649 was a phase 3, multicenter, randomized (1:1), open-label trial of OPDIVO 360 mg IV infusion over 30 minutes in combination with CapeOX q3w, or OPDIVO 240 mg IV infusion over 30 minutes in combination with FOLFOX‖ q2w (all comers*: n=789, PD-L1 CPS ≥5 population: n=473), compared with CapeOX q3w or FOLFOX q2w alone (all comers*: n=792, PD-L1 CPS ≥5 population: n=482) in previously untreated patients with unresectable, advanced or metastatic non-HER2+ gastric, gastroesophageal junction, or esophageal adenocarcinoma. Patients were stratified by tumor cell PD-L1 status, region, ECOG PS, and chemotherapy regimen, and treatment was continued until disease progression, unacceptable toxicity, or up to 2 years. The primary endpoints, assessed in patients with PD-L1 CPS ≥5, were PFS¶ and OS. Secondary endpoints included OS in patients with PD-L1 CPS ≥1 and in all comers,* and ORR¶# in all comers.* Since OS in the PD-L1 CPS ≥5 population was statistically significant, OS in PD-L1 CPS ≥1, followed by OS in all comers,* were tested hierarchically.[1,2]

OPDIVO (10 mg/mL) is an injection for IV use.[1]

*All comers refers to all randomized patients in Checkmate 649.[1] †FOLFOX or CapeOX.[1] ‡In combination with fluoropyrimidine- and platinum-containing chemotherapy.[1] §In 1L patients with metastatic gastric, GEJ, and esophageal adenocarcinomas.[1] ‖mFOLFOX6 (leucovorin, fluorouracil, and oxaliplatin) regimen was given in Checkmate 649.[1] ¶Assessed using blinded independent central review (BICR).[1] #Based on confirmed response.[1]

1L=first line; chemo=chemotherapy; CPS=combined positive score; EAC=esophageal adenocarcinoma; ECOG PS=Eastern Cooperative Oncology Group Performance Status; GC=gastric cancer; GEJ=gastroesophageal junction; GEJC=GEJ cancer; HER2=human epidermal growth factor receptor 2; IV=intravenous; K-M=Kaplan-Meier; mOS=median OS; mPFS=median PFS; ORR=overall response rate; OS=overall survival; PD-L1=programmed death ligand 1; PFS=progression-free survival; q2w=every 2 weeks; q3w=every 3 weeks.

SELECT IMPORTANT SAFETY INFORMATION

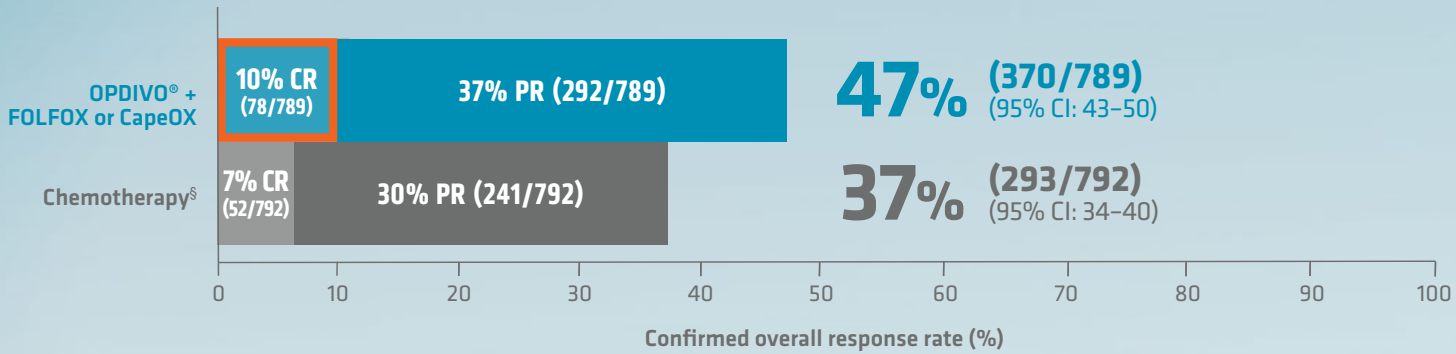
Serious Adverse Reactions

- In Checkmate 577, serious adverse reactions occurred in 33% of patients receiving OPDIVO (n=532). A serious adverse reaction reported in ≥2% of patients who received OPDIVO was pneumonitis. A fatal reaction of myocardial infarction occurred in one patient who received OPDIVO. In Checkmate 649, serious adverse reactions occurred in 52% of patients treated with OPDIVO in combination with chemotherapy (n=782). The most frequent serious adverse reactions reported in ≥2% of patients treated with OPDIVO in combination with chemotherapy were vomiting (3.7%), pneumonia (3.6%), anemia (3.6%), pyrexia (2.8%), diarrhea (2.7%), febrile neutropenia (2.6%), and pneumonitis (2.4%). Fatal adverse reactions occurred in 16 (2.0%) patients who were treated with OPDIVO in combination with chemotherapy; these included pneumonitis (4 patients), febrile neutropenia (2 patients), stroke (2 patients), gastrointestinal toxicity, intestinal mucositis, septic shock, pneumonia, infection, gastrointestinal bleeding, mesenteric vessel thrombosis, and disseminated intravascular coagulation.

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

Overall response rate (secondary endpoint) in all comers[1*†‡]



Duration of response[1*†‖]

- **mDOR in all comers‡: 8.5 mos** (95% CI: 7.2–9.9; range 1.0+ to 29.6+ mos) with OPDIVO + FOLFOX or CapeOX vs **6.9 mos** (95% CI: 5.8–7.2; range 1.2+ to 30.8+ mos) with chemotherapy§ alone

Dosage and administration

Only OPDIVO offers q2w and q3w dosing, designed to match your chemo preferences in 1L patients with metastatic GC, GEJC, and EAC[1]

Flexible dosing with fluoropyrimidine- and platinum-containing chemotherapy

OPDIVO 240 mg **q2w** (30 minute IV infusion) **with q2w chemo**

OR

OPDIVO 360 mg **q3w** (30 minute IV infusion) **with q3w chemo**

Continue treatment until disease progression, unacceptable toxicity, or up to 2 years

- The recommended dose of OPDIVO is[1]:
  - 360 mg q3w (30-minute IV infusion) with fluoropyrimidine- and platinum-containing chemotherapy q3w, or
  - 240 mg q2w (30-minute IV infusion) with fluoropyrimidine- and platinum-containing chemotherapy q2w
  - Continue treatment until disease progression, unacceptable toxicity, or up to 2 years

In the Checkmate 649 trial design,¶ in the OPDIVO + chemotherapy arm, patients who discontinued chemotherapy were permitted to receive OPDIVO monotherapy at 240 mg q2w, 360 mg q3w, or 480 mg q4w# up to 2 years after treatment initiation[1]

- Refer to the respective Prescribing Information for each therapeutic agent administered in combination with OPDIVO for the recommended dosage and administration information, as appropriate
- Administer OPDIVO first, followed by fluoropyrimidine- and platinum-containing chemotherapy on the same day[1]

*Based on the Checkmate 649 trial design, see OPDIVO Full Prescribing Information, section 14.12.[1] †The OPDIVO 480 mg q4w dosing was included as an option in the Checkmate 649 trial design; OPDIVO 480 mg q4w is not an approved dose for this indication (see OPDIVO Full Prescribing Information section 2.2).[1]

1L=first line; chemo=chemotherapy; CI=confidence interval; CR=complete response; EAC=esophageal adenocarcinoma; GC=gastric cancer; GEJC=gastroesophageal junction cancer; IV=intravenous; mDOR=median duration of response; mo=month; PR=partial response; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

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%).

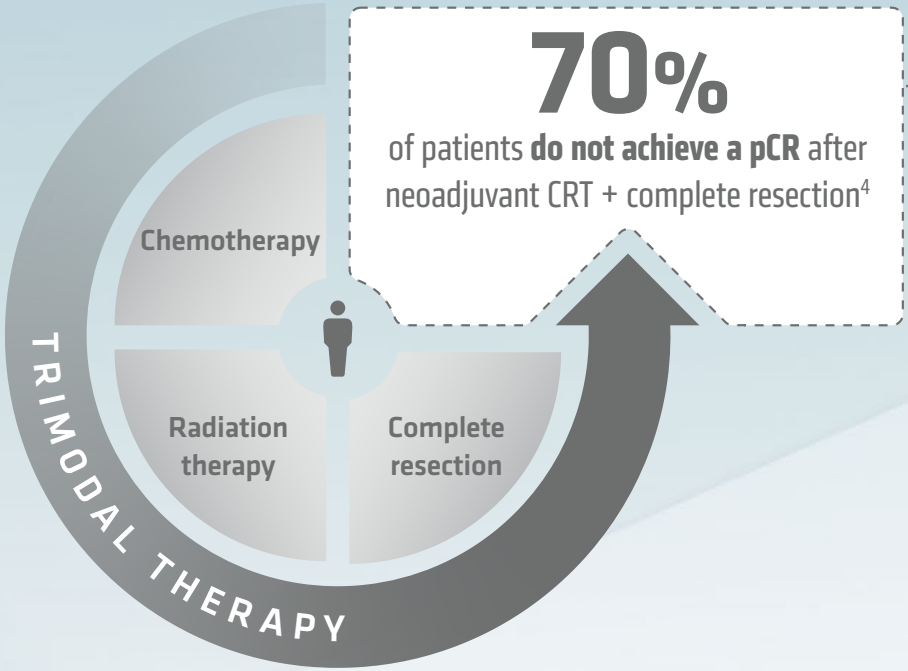
Immune-Mediated Hepatitis and Hepatotoxicity

- 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%).

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

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

Despite the benefits of trimodal therapy in EC/GEJC, patients who do not achieve a pCR may face a high risk of recurrence[3,4]



70%
of patients **do not achieve a pCR** after neoadjuvant CRT + complete resection[4]

42%–67% of patients who did not achieve a pCR experienced recurrence[4]

OPDIVO® (nivolumab)

NOW APPROVED FOR PATIENTS AT HIGH RISK OF RECURRENCE[1,3]

CRT=chemoradiotherapy; EC=esophageal cancer; GEJC=gastroesophageal junction cancer; pCR=pathologic complete response.

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 on page 6.

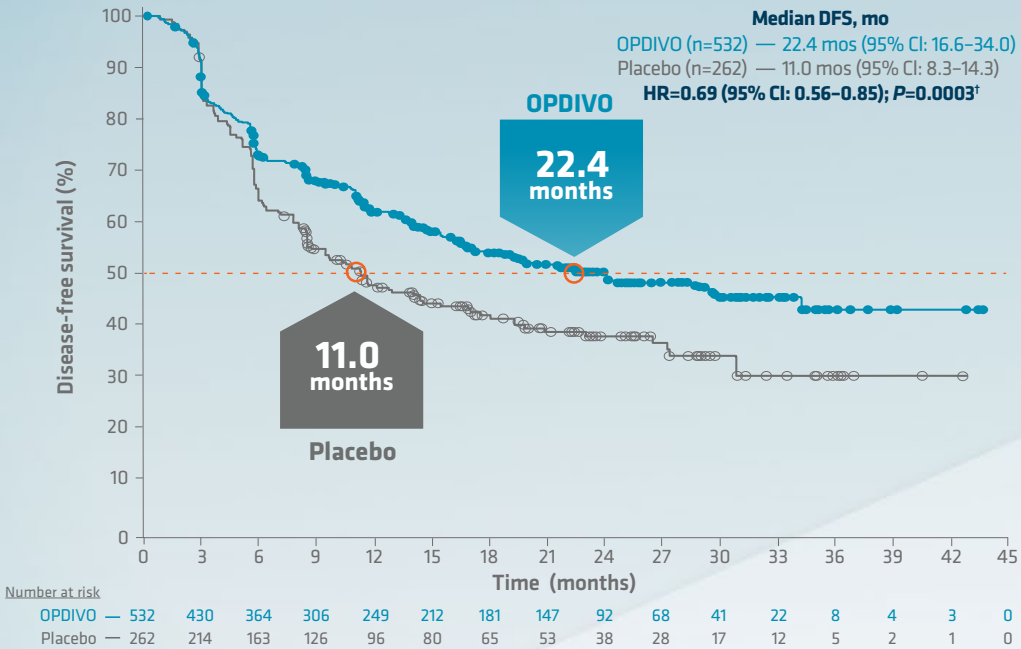
Please see additional Important Safety Information for OPDIVO throughout and US Full Prescribing Information for OPDIVO.

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

In the adjuvant treatment of patients with completely resected EC or GEJC with residual pathologic disease following neoadjuvant CRT

OPDIVO® (nivolumab) is the first and only adjuvant immunotherapy to double median disease-free survival vs placebo[1,3]

Median disease-free survival* in all randomized patients



31% reduction in the risk of recurrence or death with OPDIVO vs placebo[1]

DFS benefit observed regardless of histology[1,3]

- **Adenocarcinoma: 19.4 mos** (95% CI: 15.9–29.4) in patients receiving OPDIVO (n=376) vs **11.1 mos** (95% CI: 8.3–16.8) for patients receiving placebo (n=187); HR=0.75 (95% CI: 0.59–0.96)[3]
- **Squamous cell carcinoma: 29.7 mos** (95% CI: 14.4–NA) in patients receiving OPDIVO (n=155) vs **11.0 mos** (95% CI: 7.6–17.8) for patients receiving placebo (n=75); HR=0.61 (95% CI: 0.42–0.88)[3]
- Based on an exploratory analysis[3]

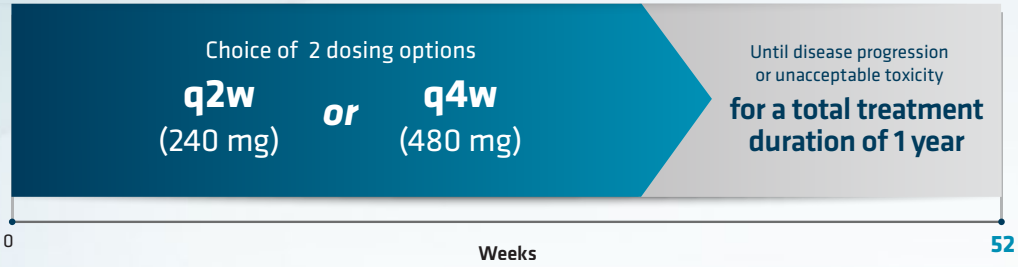
DFS benefit was observed regardless of tumor PD-L1 expression[3]

- **PD-L1 ≥1% (n=129) mDFS 19.7 mos:** (95% CI: 11.3–NA) in patients receiving OPDIVO vs **14.1 mos** (95% CI: 5.5–22.8) for patients receiving placebo; unstratified HR=0.75 (95% CI: 0.45–1.24)[3,5]
- **PD-L1 <1% (n=570) mDFS 21.3 mos:** (95% CI: 16.3–34.0) in patients receiving OPDIVO vs **11.1 mos** (95% CI: 8.3–15.2) for patients receiving placebo; unstratified HR=0.73 (95% CI: 0.57–0.92)[3,5]
- **PD-L1 indeterminate/non-evaluable (n=95):** not reached in patients receiving OPDIVO vs **9.5 mos** for patients receiving placebo; unstratified HR=0.54 (95% CI: 0.27–1.05)[3,5]
- Based on an exploratory analysis[3]

Checkmate 577 trial design: Checkmate 577 was a global, phase 3, randomized (2:1), double-blind trial evaluating OPDIVO (n=532) vs placebo (n=262) in patients with completely resected esophageal or gastroesophageal junction cancer who had residual pathologic disease following CRT. Key eligibility criteria included stage II/III EC or GEJC; adenocarcinoma or squamous cell carcinoma; residual pathologic disease ≥ypT1 or ≥ypN1; and ECOG PS of 0 or 1. Patients were stratified by tumor PD-L1 status, pathologic lymph node status, and histology. Patients received either OPDIVO 240 mg IV infusion over 30 minutes or placebo IV infusion over 30 minutes every 2 weeks for 16 weeks, followed by OPDIVO 480 mg IV infusion over 30 minutes or placebo IV infusion over 30 minutes every 4 weeks until disease recurrence, unacceptable toxicity, or for up to 1 year in total duration. The primary endpoint was disease-free survival.[1,3]*

Dosage and administration

Flexible dosing schedules to meet the needs of your patients[1]



- OPDIVO is administered over 30 minutes as an intravenous infusion[1]
- Based on exploratory dose exposure-response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[6]

*Per investigator assessment.[1] †The boundary for statistical significance at the pre-specified interim analysis required the *P* value to be less than 0.036.[3]

CI=confidence interval; CRT=chemoradiotherapy; DFS=disease-free survival; EC=esophageal cancer; ECOG PS=Eastern Cooperative Oncology Group Performance Status; GEJC=gastroesophageal junction cancer; HR=hazard ratio; IV=intravenous; mDFS=median DFS; mo=month; NA=not available; PD-L1=programmed death ligand 1; q2w=every 2 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

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%).

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

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

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.

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.

(continued on next page)

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

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

IMPORTANT SAFETY INFORMATION (CONT'D)

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

Other Immune-Mediated Adverse Reactions (cont'd)

- 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 577, serious adverse reactions occurred in 33% of patients receiving OPDIVO (n=532). A serious adverse reaction reported in ≥2% of patients who received OPDIVO was pneumonitis. A fatal reaction of myocardial infarction occurred in one patient who received OPDIVO. In Checkmate 649, serious adverse reactions occurred in 52% of patients treated with OPDIVO in combination with chemotherapy (n=782). The most frequent serious adverse reactions reported in ≥2% of patients treated with OPDIVO in combination with chemotherapy were vomiting (3.7%), pneumonia (3.6%), anemia (3.6%), pyrexia (2.8%), diarrhea (2.7%), febrile neutropenia (2.6%), and pneumonitis (2.4%). Fatal adverse reactions occurred in 16 (2.0%) patients who were treated with OPDIVO in combination with chemotherapy; these included pneumonitis (4 patients), febrile neutropenia (2 patients), stroke (2 patients), gastrointestinal toxicity, intestinal mucositis, septic shock, pneumonia, infection, gastrointestinal bleeding, mesenteric vessel thrombosis, and disseminated intravascular coagulation.

Common Adverse Reactions

- In Checkmate 577, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=532) were fatigue (34%), diarrhea (29%), nausea (23%), rash (21%), musculoskeletal pain (21%), and cough (20%). In Checkmate 649, the most common adverse reactions (≥20%) in patients treated with OPDIVO in combination with chemotherapy (n=782) were peripheral neuropathy (53%), nausea (48%), fatigue (44%), diarrhea (39%), vomiting (31%), decreased appetite (29%), abdominal pain (27%), constipation (25%), and musculoskeletal pain (20%).

References: 1. OPDIVO [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2021. **2.** Moehler M, Shitara K, Garrido M, et al. Nivolumab plus chemotherapy as first-line treatment for advanced gastric cancer/esophageal adenocarcinoma: first results of the CheckMate 649 study. Presentation at ESMO 2020. Presentation LBA6. **3.** Kelly RJ, Ajani JA, Kuzdzal J, Zander T, et al. Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer. *N Eng J Med*. 2021;384(13):1191-1203. **4.** Reynolds JV, Muldoon C, Hollywood D, Ravi N, et al. Long-term outcomes following neoadjuvant chemoradiotherapy for esophageal cancer. *Ann Surg*. 2007;2455:707-716. **5.** Data on file. NIVO 612. Princeton, NJ: Bristol-Myers Squibb Company; 2020. **6.** Long GV, Tykodi SS, Schneider JG, et al. Assessment of nivolumab exposure and clinical safety of 480 mg every 4 weeks flat-dosing schedule in patients with cancer. *J Ann Oncol*. 2018;29(11):2208-2213.

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

Bristol Myers Squibb™

OPDIVO® (nivolumab)

INJECTION FOR INTRAVENOUS USE 10 mg/mL

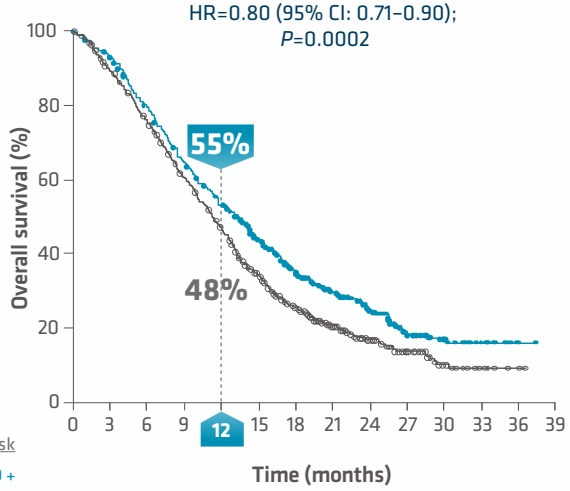
CLOSE

In 1L patients with metastatic GC, GEJC, and EAC

Superior overall survival was achieved vs chemo* in all comers,† PD-L1 CPS ≥1, and PD-L1 CPS ≥5[1,2]

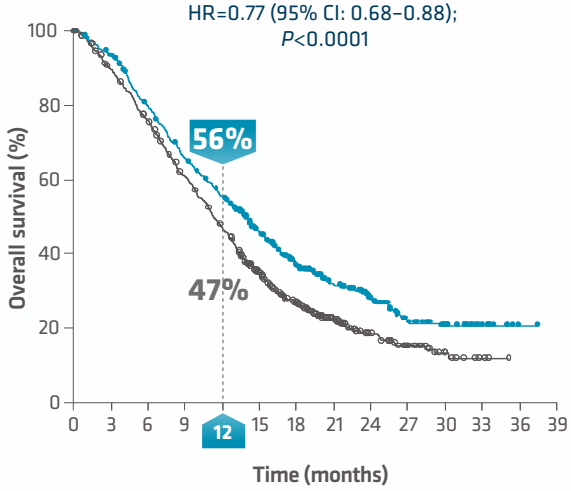
All-comers† median OS‡

OPDIVO® + FOLFOX or CapeOX (n=789) – **13.8 mos** (95% CI: 12.6–14.6)
Chemotherapy‖ (n=792) – **11.6 mos** (95% CI: 10.9–12.5)
HR=0.80 (95% CI: 0.71–0.90); *P*=0.0002



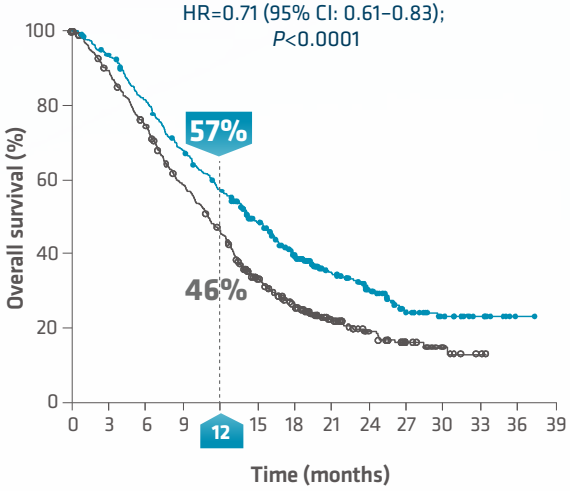
PD-L1 CPS ≥1 median OS‡

OPDIVO + FOLFOX or CapeOX (n=641) – **14.0 mos** (95% CI: 12.6–15.0)
Chemotherapy‖ (n=655) – **11.3 mos** (95% CI: 10.6–12.3)
HR=0.77 (95% CI: 0.68–0.88); *P*<0.0001



PD-L1 CPS ≥5 median OS§

OPDIVO + FOLFOX or CapeOX (n=473) – **14.4 mos** (95% CI: 13.1–16.2)
Chemotherapy‖ (n=482) – **11.1 mos** (95% CI: 10.0–12.1)
HR=0.71 (95% CI: 0.61–0.83); *P*<0.0001



Number at risk

OPDIVO + FOLFOX or CapeOX	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemotherapy‖	792	697	586	469	359	239	160	94	59	35	15	7	2	0

OPDIVO + FOLFOX or CapeOX	641	595	502	412	344	254	183	118	80	40	28	11	1	0
Chemotherapy‖	655	575	483	383	292	194	131	77	45	25	10	3	0	0

OPDIVO + FOLFOX or CapeOX	473	438	377	313	261	198	149	96	65	33	22	9	1	0
Chemotherapy‖	482	421	350	271	211	138	98	56	34	19	8	2	0	0

- All OS measures were part of the hierarchical OS testing in the trial and achieved statistical significance. The individual results were not meant to be compared[1,2]
- The 12-month OS-rate analysis was exploratory and not pre-specified within the study protocol[2]

Exploratory analysis in the PD-L1 CPS <1 population[1,2]:

- In an exploratory analysis in patients with PD-L1 CPS <1 (n=265), the median OS was **13.1 months** (95% CI: 9.8–16.7) for the OPDIVO® (nivolumab) and chemotherapy‖ arm and **12.5 months** (95% CI: 10.1–13.8) for the chemotherapy‖ arm, with a stratified HR=0.85 (95% CI: 0.63–1.15)

*OPDIVO + FOLFOX or CapeOX vs FOLFOX or CapeOX alone.[1] †All comers refers to all randomized patients in Checkmate 649.[1] ‡§Secondary endpoint. §Primary endpoint. ‖FOLFOX or CapeOX.[1]

1L=first line; CI=confidence interval; CPS=combined positive score; EAC=esophageal adenocarcinoma; GC=gastric cancer; GEJC=gastroesophageal junction cancer; HR=hazard ratio; mos=months; OS=overall survival; PD-L1=programmed death ligand 1.

SELECT IMPORTANT SAFETY INFORMATION

Serious Adverse Reactions

- In Checkmate 649, serious adverse reactions occurred in 52% of patients treated with OPDIVO in combination with chemotherapy. OPDIVO and/or chemotherapy were discontinued in 44% of patients and at least one dose was withheld in 76% of patients due to an adverse reaction. The most frequent serious adverse reactions reported in ≥2% of patients treated with OPDIVO in combination with chemotherapy were vomiting (3.7%), pneumonia (3.6%), anemia (3.6%), pyrexia (2.8%), diarrhea (2.7%), febrile neutropenia (2.6%), and pneumonitis (2.4%).

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