Interactive Dosing Guide

Dosing optimized by indication for your patients[1]

Combination therapy

OPDIVO (nivolumab) + YERVOY (ipilimumab)

OPDIVO (nivolumab) + chemotherapy

OPDIVO (nivolumab) + CABOMETYX (cabozantinib) tablets

Monotherapy

OPDIVO (nivolumab)

Fixed-dose combination therapy

Opdualag™ (nivolumab and relatlimab-rmbw)
Injection for intravenous use | 480 mg/160 mg

Important Safety Information

Important Safety Information

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO® Summary of Warnings and Precautions

- OPDIVO and YERVOY® are 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.

Opdualag™ Summary of Warnings and Precautions

- Opdualag is associated with the following Warnings and Precautions: severe and fatal immune-mediated adverse reactions including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis with renal dysfunction, dermatologic adverse reactions, myocarditis, and other immune-mediated adverse reactions; infusion-related reactions; complications of allogeneic hematopoietic stem cell transplantation (HSCT) after PD-1/PD-L1 blocking antibody; and embryo-fetal toxicity.

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® combination indications[1]

mMelanoma

GO TO DOSING

OPDIVO, in combination with YERVOY®, is indicated for the treatment of adult patients with unresectable or metastatic melanoma.

HCC

GO TO DOSING

OPDIVO, in combination with YERVOY, is indicated for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

MSI-H/dMMR mCRC

GO TO DOSING

OPDIVO, in combination with YERVOY, is indicated for the treatment of adult and pediatric patients 12 years and older with MSI-H or dMMR metastatic CRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Neoadj tx of resectable NSCLC

GO TO DOSING

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).

PD-L1 ≥1% mNSCLC

GO TO DOSING

OPDIVO, in combination with YERVOY, is indicated for the first-line treatment of adult patients with metastatic NSCLC whose tumors express PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

r/m NSCLC

GO TO DOSING

OPDIVO, in combination with YERVOY and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

(continued on next page)

OPDIVO (10 mg/mL) and YERVOY (5 mg/mL) are injections for intravenous use.[1,2]

ALK=anaplastic lymphoma kinase; CRC=colorectal cancer; dMMR=mismatch repair deficient; EGFR=epidermal growth factor receptor; mCRC=metastatic CRC; mMelanoma=metastatic melanoma; mNSCLC=metastatic NSCLC; MSI-H=microsatellite instability-high; PD-L1=programmed death ligand 1; r/m=recurrent or metastatic; uMPM=unresectable MPM.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Infusion-Related Reactions

- OPDIVO and YERVOY can cause severe infusion-related reactions. Discontinue OPDIVO and YERVOY 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. In melanoma patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 2.5% (10/407) of patients. In HCC patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 8% (4/49) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 5.1% (28/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 4.2% (5/119) of patients. In MPM patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, infusion-related reactions occurred in 12% (37/300) of patients.

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® combination indications[1] (cont'd)

uMPM

GO TO DOSING

OPDIVO, in combination with YERVOY®, is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM).

aRCC

GO TO DOSING

OPDIVO, in combination with YERVOY, is indicated for the first-line treatment of adult patients with intermediate or poor risk advanced RCC.

aRCC

GO TO DOSING

OPDIVO, in combination with CABOMETYX®, is indicated for the first-line treatment of adult patients with advanced RCC.

ESCC

GO TO DOSING

OPDIVO, in combination with YERVOY , is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

ESCC

GO TO DOSING

OPDIVO, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

Advanced or metastatic GC, GEJC, and EAC

GO TO DOSING

OPDIVO, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of adult patients with advanced or metastatic GC, GEJC, and EAC.

aRCC=advanced RCC; EAC=esophageal adenocarcinoma; GEJC=gastroesophageal junction cancer: GC=gastric cancer; RCC=renal cell carcinoma.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Infusion-Related Reactions

- OPDIVO and YERVOY can cause severe infusion-related reactions. Discontinue OPDIVO and YERVOY 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. In melanoma patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 2.5% (10/407) of patients. In HCC patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 8% (4/49) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 5.1% (28/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 4.2% (5/119) of patients. In MPM patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, infusion-related reactions occurred in 12% (37/300) of patients.

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® monotherapy indications[1]

Adj tx of melanoma

GO TO DOSING

OPDIVO is indicated for the adjuvant treatment of adult patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

mMelanoma

GO TO DOSING

OPDIVO, as a single agent, is indicated for the treatment of adult patients with unresectable or metastatic melanoma.

mNSCLC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.

aRCC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

r/p cHL

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin or after 3 or more lines of systemic therapy that includes autologous HSCT.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

r/m SCCHN

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

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Adj=adjuvant; ALK=anaplastic lymphoma kinase; aRCC=advanced RCC; EGFR=epidermal growth factor receptor; mMelanoma=metastatic melanoma; mNSCLC=metastatic NSCLC; r/m=recurrent or metastatic; r/p=relapsed or progressed; tx=treatment.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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 and YERVOY (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® monotherapy indications[1] (cont'd)

Adj tx of UC

GO TO DOSING

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

mUC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

MSI-H/dMMR mCRC

GO TO DOSING

OPDIVO, as a single agent, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

aESCC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Adj tx of EC or GEJC

GO TO DOSING

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

Adj=adjuvant; aESCC=advanced ESCC; EC=esophageal cancer; GEJC=gastroesophageal junction cancer; mCRC=metastatic CRC; mUC=metastatic urothelial carcinoma; tx=treatment.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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 and YERVOY (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

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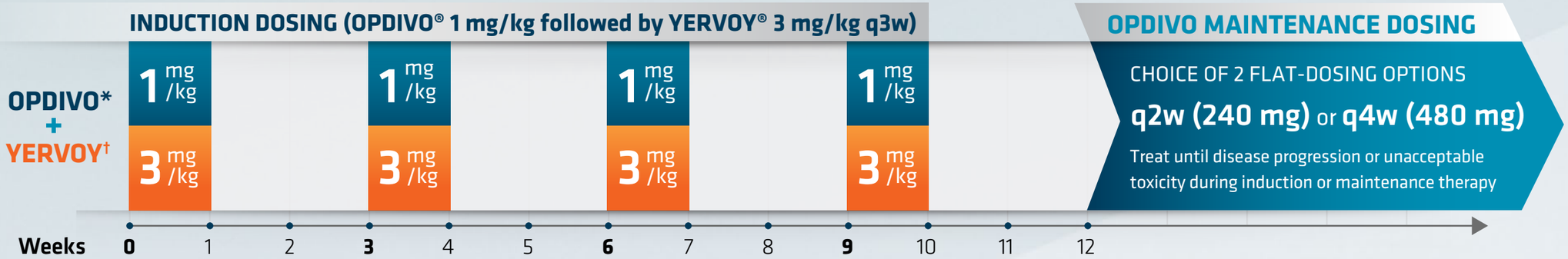
mMelanoma[1]

For adult patients with unresectable or metastatic melanoma



*OPDIVO is administered as a 30-minute IV infusion in both the induction and maintenance phases.
†YERVOY is administered as a 30-minute IV infusion.

- The first dose of OPDIVO monotherapy should be administered after completing up to a maximum of 4 doses of the OPDIVO and YERVOY combination therapy
- Based on exploratory dose exposure response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

IV=intravenous; mMelanoma=metastatic melanoma; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 067, serious adverse reactions (74% and 44%), adverse reactions leading to permanent discontinuation (47% and 18%) or to dosing delays (58% and 36%), and Grade 3 or 4 adverse reactions (72% and 51%) all occurred more frequently in the OPDIVO plus YERVOY arm (n=313) relative to the OPDIVO arm (n=313). The most frequent (≥10%) serious adverse reactions in the OPDIVO plus YERVOY arm and the OPDIVO arm, respectively, were diarrhea (13% and 2.2%), colitis (10% and 1.9%), and pyrexia (10% and 1.0%).

OPDIVO Common Adverse Reactions

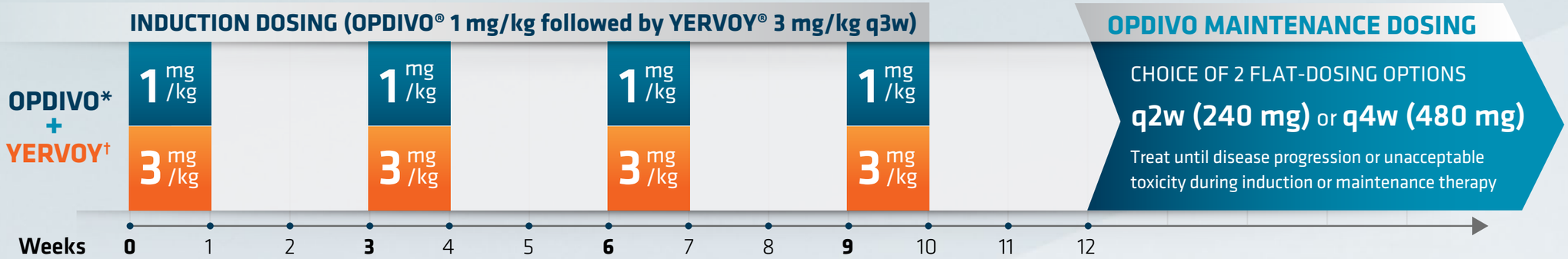
- In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO plus YERVOY arm (n=313) were fatigue (62%), diarrhea (54%), rash (53%), nausea (44%), pyrexia (40%), pruritus (39%), musculoskeletal pain (32%), vomiting (31%), decreased appetite (29%), cough (27%), headache (26%), dyspnea (24%), upper respiratory tract infection (23%), arthralgia (21%), and increased transaminases (25%). In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO arm (n=313) were fatigue (59%), rash (40%), musculoskeletal pain (42%), diarrhea (36%), nausea (30%), cough (28%), pruritus (27%), upper respiratory tract infection (22%), decreased appetite (22%), headache (22%), constipation (21%), arthralgia (21%), and vomiting (20%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

HCC[1]

In adult patients with HCC previously treated with sorafenib



*OPDIVO is administered as a 30-minute IV infusion in both the induction and maintenance phases.
†YERVOY is administered as a 30-minute IV infusion.

- The first dose of OPDIVO monotherapy should be administered after completing 4 doses of the OPDIVO and YERVOY combination therapy
- Based on exploratory dose exposure response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

HCC=hepatocellular carcinoma; IV=intravenous; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 040, serious adverse reactions occurred in 49% of patients receiving OPDIVO (n=154). The most frequent serious adverse reactions reported in ≥2% of patients were pyrexia, ascites, back pain, general physical health deterioration, abdominal pain, pneumonia, and anemia. In Checkmate 040, serious adverse reactions occurred in 59% of patients receiving OPDIVO with YERVOY (n=49). Serious adverse reactions reported in ≥4% of patients were pyrexia, diarrhea, anemia, increased AST, adrenal insufficiency, ascites, esophageal varices hemorrhage, hyponatremia, increased blood bilirubin, and pneumonitis.

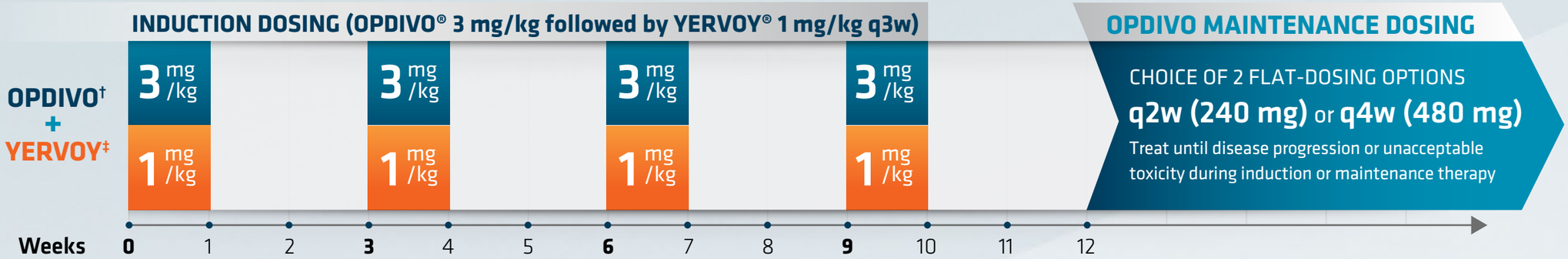
OPDIVO Common Adverse Reactions

- In Checkmate 040, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=154) were fatigue (38%), musculoskeletal pain (36%), abdominal pain (34%), pruritus (27%), diarrhea (27%), rash (26%), cough (23%), and decreased appetite (22%). In Checkmate 040, the most common adverse reactions (≥20%) in patients receiving OPDIVO with YERVOY (n=49), were rash (53%), pruritus (53%), musculoskeletal pain (41%), diarrhea (39%), cough (37%), decreased appetite (35%), fatigue (27%), pyrexia (27%), abdominal pain (22%), headache (22%), nausea (20%), dizziness (20%), hypothyroidism (20%), and weight decreased (20%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

MSI-H/dMMR mCRC[1]*

In patients (≥12 years) with MSI-H/dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan



*For MSI-H/dMMR mCRC adult and pediatric patients age 12 years and older and weighing 40 kg or more, follow OPDIVO dosing above. For pediatric patients age 12 years and older and weighing less than 40 kg, OPDIVO induction dosing is the same as the above and maintenance dosing is 3 mg/kg every 2 weeks (30-minute IV infusion).
†OPDIVO is administered as a 30-minute IV infusion in both the induction and maintenance phases.
‡YERVOY is administered as a 30-minute IV infusion.

- The first dose of OPDIVO monotherapy should be administered after completing 4 doses of the OPDIVO and YERVOY combination therapy
- Based on exploratory dose exposure response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

dMMR=mismatch repair deficient; IV=intravenous; mCRC=metastatic colorectal cancer; MSI-H=microsatellite instability-high; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY (n=119), serious adverse reactions occurred in 47% of patients. The most frequent serious adverse reactions reported in ≥2% of patients were colitis/diarrhea, hepatic events, abdominal pain, acute kidney injury, pyrexia, and dehydration.

OPDIVO Common Adverse Reactions

- In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO as a single agent (n=74), the most common adverse reactions (≥20%) were fatigue (54%), diarrhea (43%), abdominal pain (34%), nausea (34%), vomiting (28%), musculoskeletal pain (28%), cough (26%), pyrexia (24%), rash (23%), constipation (20%), and upper respiratory tract infection (20%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY (n=119), the most common adverse reactions (≥20%) were fatigue (49%), diarrhea (45%), pyrexia (36%), musculoskeletal pain (36%), abdominal pain (30%), pruritus (28%), nausea (26%), rash (25%), decreased appetite (20%), and vomiting (20%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
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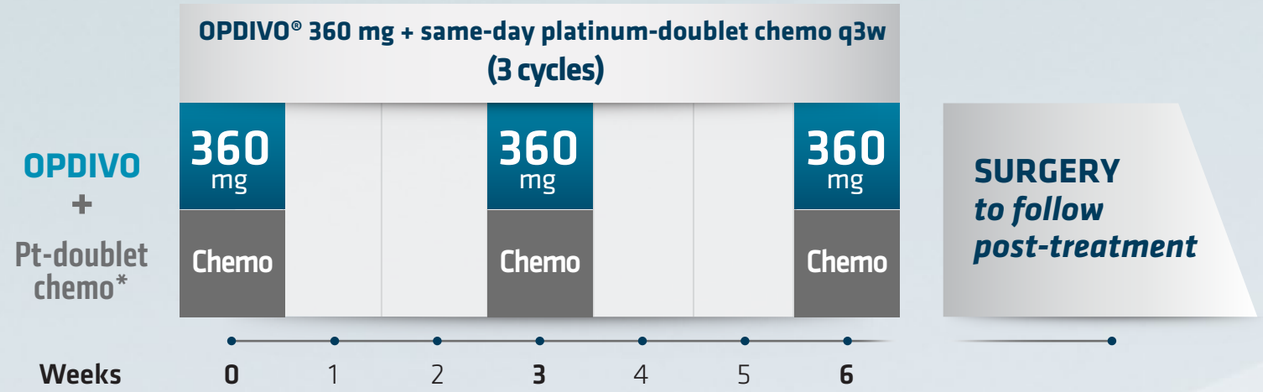
Neoadjuvant treatment of resectable NSCLC[1,4]

In adult patients with resectable NSCLC, regardless of PD-L1 expression



- OPDIVO is administered as an IV infusion over 30 minutes
- 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*
- No premedication required with OPDIVO

*Platinum-doublet chemotherapy consisted of paclitaxel 175 mg/m² or 200 mg/m² and carboplatin AUC 5 or AUC 6 (any histology); pemetrexed 500 mg/m² and cisplatin 75 mg/m² (non-squamous histology); or gemcitabine 1000 mg/m² or 1250 mg/m² and cisplatin 75 mg/m² (squamous histology). In the platinum-doublet chemotherapy arm, two additional treatment regimen options included vinorelbine 25 mg/m² or 30 mg/m² and cisplatin 75 mg/m²; or docetaxel 60 mg/m² or 75 mg/m² and cisplatin 75 mg/m² (any histology).[1]
AUC=area under the curve; chemo=chemotherapy; IV=intravenous; NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1; Pt=platinum; q3w=every 3 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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.

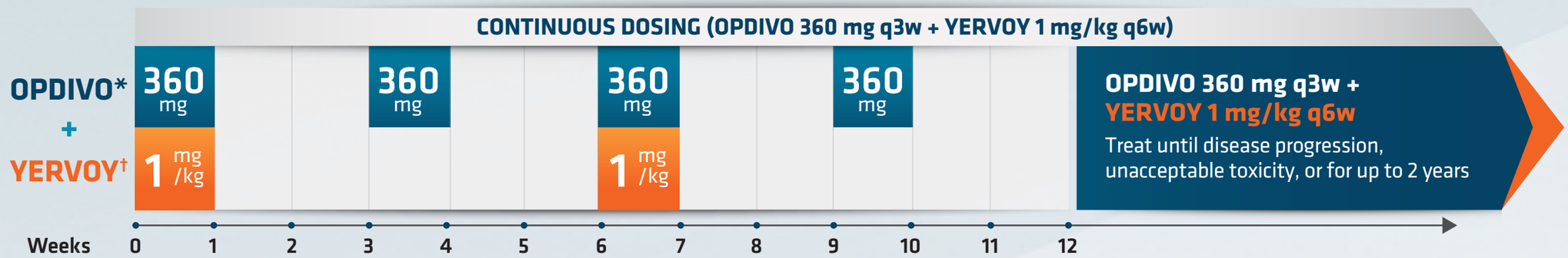
OPDIVO Common Adverse Reactions

- 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 additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

PD-L1 ≥1% mNSCLC[1]

In certain patients with PD-L1 ≥1% mNSCLC



*OPDIVO is administered as an IV infusion over 30 minutes.
†YERVOY is administered as an IV infusion over 30 minutes.

- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

IV=intravenous; mNSCLC=metastatic non-small cell lung cancer; PD-L1=programmed death ligand 1; q3w=every 3 weeks; q6w=every 6 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 227, serious adverse reactions occurred in 58% of patients (n=576). The most frequent (≥2%) serious adverse reactions were pneumonia, diarrhea/colitis, pneumonitis, hepatitis, pulmonary embolism, adrenal insufficiency, and hypophysitis. Fatal adverse reactions occurred in 1.7% of patients; these included events of pneumonitis (4 patients), myocarditis, acute kidney injury, shock, hyperglycemia, multi-system organ failure, and renal failure.

OPDIVO Common Adverse Reactions

- In Checkmate 227, the most common (≥20%) adverse reactions were fatigue (44%), rash (34%), decreased appetite (31%), musculoskeletal pain (27%), diarrhea/colitis (26%), dyspnea (26%), cough (23%), hepatitis (21%), nausea (21%), and pruritus (21%).

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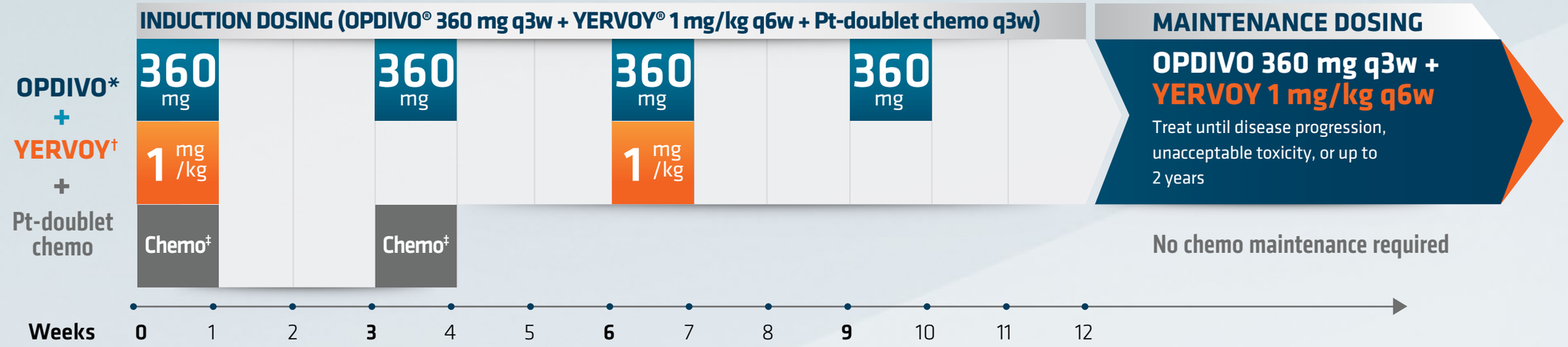
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

r/m NSCLC[1]

In certain adult patients with r/m NSCLC



*OPDIVO is administered as an IV infusion over 30 minutes.
†YERVOY is administered as an IV infusion over 30 minutes.
‡Histology-based chemo; SQ patients: carboplatin AUC 6 + paclitaxel 200 mg/m^2 q3w; NSQ patients: carboplatin AUC 5 or 6 or cisplatin 75 mg/m^2 + pemetrexed 500 mg/m^2 q3w.

- On the first week, 4 agents will be administered (OPDIVO 360 mg + YERVOY 1 mg/kg + histology-based chemo‡), followed by 3 agents (OPDIVO + histology-based chemo‡) on the third week, 2 agents (OPDIVO + YERVOY) on the sixth week, and OPDIVO monotherapy on the ninth week, followed by maintenance therapy of OPDIVO + YERVOY
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

AUC=area under the curve; chemo=chemotherapy; IV=intravenous; NSCLC=non-small cell lung cancer; NSQ=non-squamous; Pt=platinum; q3w=every 3 weeks; q6w=every 6 weeks; r/m=recurrent or metastatic; SQ=squamous.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 9LA, serious adverse reactions occurred in 57% of patients (n=358). The most frequent (>2%) serious adverse reactions were pneumonia, diarrhea, febrile neutropenia, anemia, acute kidney injury, musculoskeletal pain, dyspnea, pneumonitis, and respiratory failure. Fatal adverse reactions occurred in 7 (2%) patients, and included hepatic toxicity, acute renal failure, sepsis, pneumonitis, diarrhea with hypokalemia, and massive hemoptysis in the setting of thrombocytopenia.

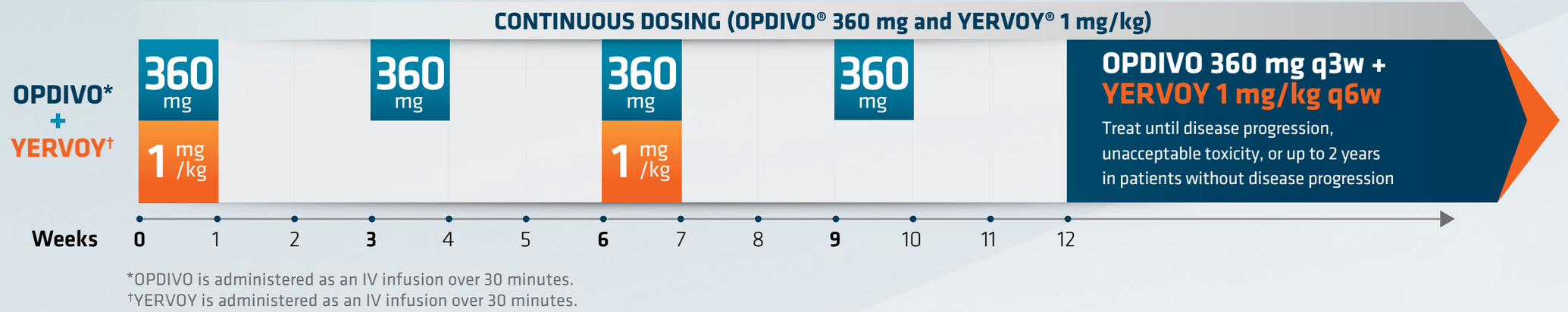
OPDIVO Common Adverse Reactions

- In Checkmate 9LA, the most common (>20%) adverse reactions were fatigue (49%), musculoskeletal pain (39%), nausea (32%), diarrhea (31%), rash (30%), decreased appetite (28%), constipation (21%), and pruritus (21%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

uMPM[1]

In certain patients with uMPM



*OPDIVO is administered as an IV infusion over 30 minutes.
†YERVOY is administered as an IV infusion over 30 minutes.

- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

IV=intravenous; q3w=every 3 weeks; q6w=every 6 weeks; uMPM=unresectable malignant pleural mesothelioma.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 743, serious adverse reactions occurred in 54% of patients receiving OPDIVO plus YERVOY. The most frequent serious adverse reactions reported in ≥2% of patients were pneumonia, pyrexia, diarrhea, pneumonitis, pleural effusion, dyspnea, acute kidney injury, infusion-related reaction, musculoskeletal pain, and pulmonary embolism. Fatal adverse reactions occurred in 4 (1.3%) patients and included pneumonitis, acute heart failure, sepsis, and encephalitis.

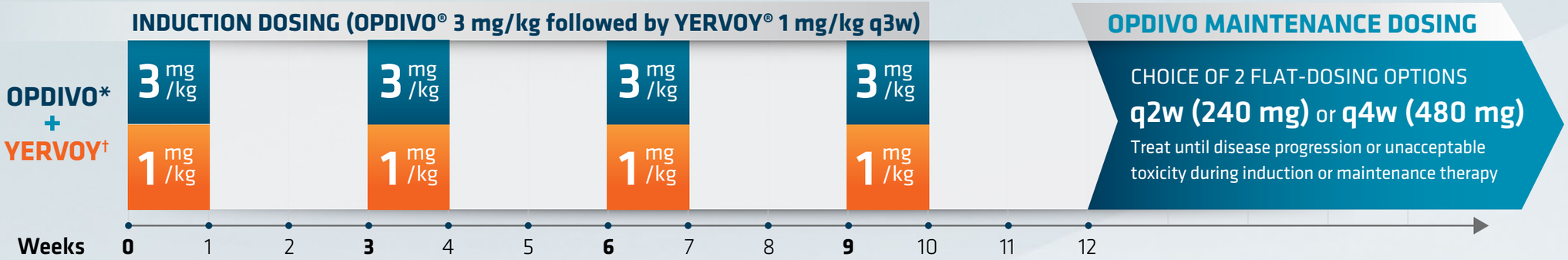
OPDIVO Common Adverse Reactions

- In Checkmate 743, the most common adverse reactions (≥20%) in patients receiving OPDIVO plus YERVOY were fatigue (43%), musculoskeletal pain (38%), rash (34%), diarrhea (32%), dyspnea (27%), nausea (24%), decreased appetite (24%), cough (23%), and pruritus (21%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

aRCC[1]

In adult patients with intermediate or poor risk, previously untreated aRCC



*OPDIVO is administered as a 30-minute IV infusion in both the induction and maintenance phases.
†YERVOY is administered as a 30-minute IV infusion.

- The first dose of OPDIVO monotherapy should be administered after completing 4 doses of the OPDIVO and YERVOY combination therapy
- Based on exploratory dose exposure response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

aRCC=advanced renal cell carcinoma; IV=intravenous; q2w=every 2 weeks; q3w-=every 3 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 214, serious adverse reactions occurred in 59% of patients receiving OPDIVO plus YERVOY (n=547). The most frequent serious adverse reactions reported in ≥2% of patients were diarrhea, pyrexia, pneumonia, pneumonitis, hypophysitis, acute kidney injury, dyspnea, adrenal insufficiency, and colitis.

OPDIVO Common Adverse Reactions

- In Checkmate 214, the most common adverse reactions (≥20%) reported in patients treated with OPDIVO plus YERVOY (n=547) were fatigue (58%), rash (39%), diarrhea (38%), musculoskeletal pain (37%), pruritus (33%), nausea (30%), cough (28%), pyrexia (25%), arthralgia (23%), decreased appetite (21%), dyspnea (20%), and vomiting (20%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

ESCC[1]

In the 1L treatment of patients with advanced or metastatic ESCC

OPDIVO + YERVOY

OPDIVO 3 mg/kg **q2w** (30 minute IV infusion)

OR

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

WITH

YERVOY 1 mg/kg **q6w** (30 minute IV infusion)

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

- The recommended dose of OPDIVO is[1]:
  - 3 mg/kg q2w (30-minute IV infusion) with YERVOY 1 mg/kg q6w (30-minute IV infusion), or
  - 360 mg q3w (30-minute IV infusion) with YERVOY 1 mg/kg q6w (30-minute IV infusion)
  - Continue treatment until disease progression, unacceptable toxicity, or up to 2 years
- Administer OPDIVO first, followed by YERVOY on the same day
- Review the US Full Prescribing Information for OPDIVO and YERVOY for recommended dosage information
- No premedication required with OPDIVO + YERVOY

1L=first line; ESCC=esophageal squamous cell carcinoma; IV=intravenous; q2w=every 2 weeks; q3w=every 3 weeks; q6w=every 6 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Reactions

- In Checkmate 648, serious adverse reactions occurred in 69% of patients receiving OPDIVO in combination with YERVOY (n=322). The most frequent serious adverse reactions reported in ≥2% who received OPDIVO in combination with YERVOY were pneumonia (10%), pyrexia (4.3%), pneumonitis (4.0%), aspiration pneumonia (3.7%), dysphagia (3.7%), hepatic function abnormal (2.8%), decreased appetite (2.8%), adrenal insufficiency (2.5%), and dehydration (2.5%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with YERVOY; these included pneumonitis, interstitial lung disease, pulmonary embolism, and acute respiratory distress syndrome.

OPDIVO Common Adverse Reactions

- In Checkmate 648, the most common adverse reactions reported in ≥20% of patients treated with OPDIVO in combination with YERVOY were rash (31%), fatigue (28%), pyrexia (23%), nausea (22%), diarrhea (22%), and constipation (20%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

ESCC[1]

In the 1L treatment of patients with advanced or metastatic ESCC

OPDIVO with fluoropyrimidine- and platinum-containing chemotherapy

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

OR

OPDIVO 480 mg q4w (30 minute IV infusion) **with chemo**

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

- The recommended dose of OPDIVO:
  - 240 mg q2w (30-minute IV infusion), or
  - 480 mg q4w (30-minute IV infusion)
  - Administer OPDIVO in combination with fluoropyrimidine- and platinum-containing chemotherapy.
- Refer to the respective Prescribing Information for each therapeutic agent administered in combination with OPDIVO for the recommended dosage information, as appropriate
- Administer OPDIVO first, followed by fluoropyrimidine- and platinum-containing chemotherapy on the same day

1L=first line; chemo=chemotherapy; ESCC=esophageal squamous cell carcinoma; IV=intravenous; q2w=every 2 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Reactions

- In Checkmate 648, serious adverse reactions occurred in 62% of patients receiving OPDIVO in combination with chemotherapy (n=310). The most frequent serious adverse reactions reported in ≥2% of patients who received OPDIVO with chemotherapy were pneumonia (11%), dysphagia (7%), esophageal stenosis (2.9%), acute kidney injury (2.9%), and pyrexia (2.3%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with chemotherapy; these included pneumonitis, pneumatosis intestinalis, pneumonia, and acute kidney injury.

OPDIVO Serious Reactions

- In Checkmate 648, the most common adverse reactions (≥20%) in patients treated with OPDIVO in combination with chemotherapy (n=310) were nausea (65%), decreased appetite (51%), fatigue (47%), constipation (44%), stomatitis (44%), diarrhea (29%), and vomiting (23%).

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

Advanced or metastatic GC, GEJC, and EAC[1]

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

OPDIVO 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:

- 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
- 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

1L=first line; chemo=chemotherapy; EAC=esophageal adenocarcinoma; GC=gastric cancer; GEJC=gastroesophageal cancer; IV=intravenous; q2w=every 2 weeks; q3w=every 3 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- 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.

OPDIVO Common Adverse Reactions

- 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%).

Please see additional Important Safety Information for OPDIVO and YERVOY® (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

aRCC[1]

In certain patients with aRCC

DOSING

OPDIVO®* + CABOMETYX®

CHOICE OF 2 DOSING OPTIONS

q2w (240 mg) or **q4w** (480 mg) **IV***

(until disease progression, unacceptable toxicity, or up to 2 years)

ONCE-DAILY TABLET (40 mg)

(without food, until disease progression or unacceptable toxicity)

*OPDIVO is administered as an IV infusion over 30 minutes.

- Based on exploratory dose exposure response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- In combination with OPDIVO, the recommended starting dose for CABOMETYX is 40 mg. In Checkmate 9ER, CABOMETYX could be interrupted or reduced to 20 mg daily or 20 mg every other day[1]
- Review the US Full Prescribing Information for both OPDIVO and CABOMETYX prior to initiation, including recommended dosage and modifications
- No premedication required with OPDIVO + CABOMETYX

aRCC=advanced renal cell carcinoma; IV=intravenous; q2w=every 2 weeks; q4w=every 4 weeks.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Serious Adverse Reactions

- In Checkmate 9ER, serious adverse reactions occurred in 48% of patients receiving OPDIVO and cabozantinib (n=320). The most frequent serious adverse reactions reported in ≥2% of patients were diarrhea, pneumonia, pneumonitis, pulmonary embolism, urinary tract infection, and hyponatremia. Fatal intestinal perforations occurred in 3 (0.9%) patients.

OPDIVO Common Adverse Reactions

- In Checkmate 9ER, the most common adverse reactions (≥20%) in patients receiving OPDIVO and cabozantinib (n=320) were diarrhea (64%), fatigue (51%), hepatotoxicity (44%), palmar-plantar erythrodysaesthesia syndrome (40%), stomatitis (37%), rash (36%), hypertension (36%), hypothyroidism (34%), musculoskeletal pain (33%), decreased appetite (28%), nausea (27%), dysgeusia (24%), abdominal pain (22%), cough (20%) and upper respiratory tract infection (20%).

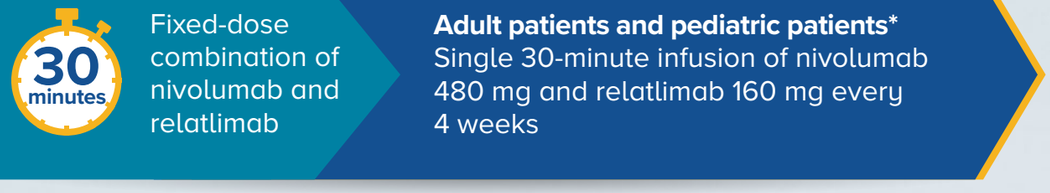
Please see additional Important Safety Information for OPDIVO and YERVOY (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

Unresectable or metastatic melanoma[5]

Opdualag™ is indicated for the treatment of adults and pediatric patients 12 years of age or older with unresectable or metastatic melanoma.

Fixed-dose combination of nivolumab and relatlimab administered as a 30-minute intravenous infusion every 4 weeks



*12 years of age or older who weigh at least 40 kg. A recommended dosage for pediatric patients 12 years of age or older who weigh less than 40 kg and pediatric patients younger than 12 years of age has not been established.

- Opdualag is a fixed-dose combination: a co-formulation of 2 active ingredients in a single vial administered as a single infusion
- A single-dose vial contains 240 mg of nivolumab and 80 mg of relatlimab per 20 mL (one dose will require 2 vials)

Opdualag (nivolumab 12 mg/mL and relatlimab-rmbw 4 mg/mL) is an injection for intravenous use.

SELECT IMPORTANT SAFETY INFORMATION

Opdualag Serious Adverse Reactions

- In Relativity-047, fatal adverse reaction occurred in 3 (0.8%) patients who were treated with Opdualag; these included hemophagocytic lymphohistiocytosis, acute edema of the lung, and pneumonitis. Serious adverse reactions occurred in 36% of patients treated with Opdualag. The most frequent serious adverse reactions reported in ≥1% of patients treated with Opdualag were adrenal insufficiency (1.4%), anemia (1.4%), colitis (1.4%), pneumonia (1.4%), acute myocardial infarction (1.1%), back pain (1.1%), diarrhea (1.1%), myocarditis (1.1%), and pneumonitis (1.1%).

Opdualag Common Adverse Reactions and Laboratory Abnormalities

- The most common adverse reactions reported in ≥20% of the patients treated with Opdualag were musculoskeletal pain (45%), fatigue (39%), rash (28%), pruritus (25%), and diarrhea (24%).
- The most common laboratory abnormalities that occurred in ≥20% of patients treated with Opdualag were decreased hemoglobin (37%), decreased lymphocytes (32%), increased AST (30%), increased ALT (26%), and decreased sodium (24%).

Please see additional Important Safety Information for OPDIVO® (nivolumab) and YERVOY® (ipilimumab) on pages 23–28, for Opdualag on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trial.

OPDIVO® monotherapy indications[1]

Adj tx of melanoma

GO TO DOSING

OPDIVO is indicated for the adjuvant treatment of adult patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

mMelanoma

GO TO DOSING

OPDIVO, as a single agent, is indicated for the treatment of adult patients with unresectable or metastatic melanoma.

mNSCLC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.

aRCC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

r/p cHL

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin or after 3 or more lines of systemic therapy that includes autologous HSCT.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

r/m SCCHN

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

(continued on next page)

Adj=adjuvant; ALK=anaplastic lymphoma kinase; aRCC=advanced RCC; EGFR=epidermal growth factor receptor; mMelanoma=metastatic melanoma; mNSCLC=metastatic NSCLC; r/p=relapsed or progressed; tx=treatment.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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 and YERVOY® (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® monotherapy indications[1] (cont'd)

Adj tx of UC

GO TO DOSING

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

mUC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

MSI-H/dMMR mCRC

GO TO DOSING

OPDIVO, as a single agent, is indicated for the treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

aESCC

GO TO DOSING

OPDIVO is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Adj tx of EC or GEJC

GO TO DOSING

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

Adj=adjuvant; aESCC=advanced ESCC; EC=esophageal cancer; GEJC=gastroesophageal junction cancer; mCRC=metastatic CRC; mUC=metastatic urothelial carcinoma; tx=treatment.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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 and YERVOY® (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

In the adjuvant setting:

OPDIVO® (nivolumab) monotherapy dosing[1]

Adj tx of mel

Adj tx of UC

Adj tx of EC or GEJC

Choice of 2 dosing options

q2w 240 mg **OR** **q4w** 480 mg

Treat until disease recurrence or unacceptable toxicity for **up to 1 year**

Treat until disease progression or unacceptable toxicity for a **total treatment duration of 1 year**

- OPDIVO is administered over 30 minutes as an intravenous infusion
- Based on exploratory dose exposure-response relationships for efficacy and safety, OPDIVO 240 mg q2w and 480 mg q4w are predicted to be similar[3]
- Review the Full US Prescribing Information for recommended dosage information for OPDIVO
- No premedication required

Adj=adjuvant; EC=esophageal cancer; GEJC=gastroesophageal junction cancer; IV=intravenous; q2w=every 2 weeks; q4w=every 4 weeks; tx=treatment; UC=urothelial carcinoma.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO Infusion-Related Reactions

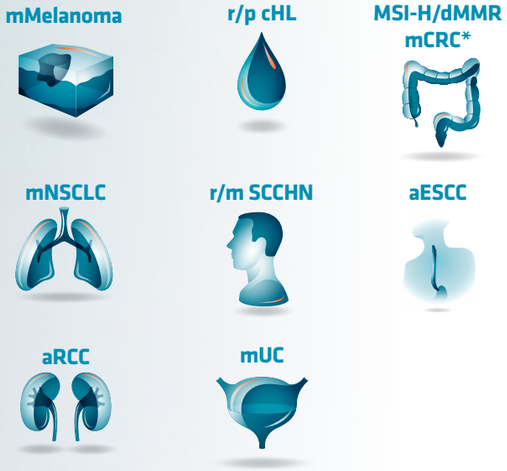
- OPDIVO can cause severe infusion-related reactions. Discontinue OPDIVO in patients with severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild (Grade 1) or moderate (Grade 2) infusion-related reactions. In patients receiving 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 and YERVOY® (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

In the advanced or metastatic setting:

OPDIVO® monotherapy dosing[1]



Dose every **2 weeks**

240 mg — Treat until unacceptable toxicity or disease progression

OR

Dose every **4 weeks**

480 mg — Treat until unacceptable toxicity or disease progression

*For MSI-H/dMMR mCRC adult and pediatric patients age 12 years and older and weighing 40 kg or more, follow OPDIVO dosing above.
For pediatric patients age 12 years and older and weighing less than 40 kg, OPDIVO dosing is 3 mg/kg every 2 weeks (30-minute IV 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[3]
- Review the US Full Prescribing Information for recommended dosage information for OPDIVO
- No premedication required

aESCC=advanced esophageal squamous cell carcinoma; aRCC=advanced renal cell carcinoma; cHL=classical Hodgkin lymphoma; dMMR=mismatch repair deficient; IV=intravenous; mCRC=metastatic colorectal cancer; mel=melanoma; mMelanoma=metastatic melanoma; mNSCLC=metastatic non-small cell lung cancer; MSI-H=microsatellite instability-high; mUC=metastatic urothelial carcinoma; q2w=every 2 weeks; q4w=every 4 weeks; r/m=recurrent or metastatic; r/p=relapsed or progressed; SCCHN=squamous cell carcinoma of the head and neck; tx=treatment.

SELECT IMPORTANT SAFETY INFORMATION

OPDIVO 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 and YERVOY® (ipilimumab) on pages 23–28, for Opdualag™ (nivolumab and relatlimab-rmbw) on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

OPDIVO® Important Safety Information

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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 or YERVOY. Early identification and management are essential to ensure safe use of OPDIVO and YERVOY. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function at baseline and periodically during treatment with OPDIVO and before each dose of YERVOY. 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 and YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if OPDIVO or YERVOY 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 and YERVOY 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%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated pneumonitis occurred in 7% (31/456) of patients, including Grade 4 (0.2%), Grade 3 (2.0%), and Grade 2 (4.4%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated pneumonitis occurred in 3.9% (26/666) of patients, including Grade 3 (1.4%) and Grade 2 (2.6%). In NSCLC patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, immune-mediated pneumonitis occurred in 9% (50/576) of patients, including Grade 4 (0.5%), Grade 3 (3.5%), and Grade 2 (4.0%). Four patients (0.7%) died due to pneumonitis.
- In Checkmate 205 and 039, pneumonitis, including interstitial lung disease, occurred in 6.0% (16/266) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 4.9% (13/266) of patients receiving OPDIVO, including Grade 3 (n=1) and Grade 2 (n=12).

Immune-Mediated Colitis

- OPDIVO and YERVOY can cause immune-mediated colitis, which may be fatal. 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%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated colitis occurred in 25% (115/456) of patients, including Grade 4 (0.4%), Grade 3 (14%) and Grade 2 (8%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated colitis occurred in 9% (60/666) of patients, including Grade 3 (4.4%) and Grade 2 (3.7%).

Immune-Mediated Hepatitis and Hepatotoxicity

- OPDIVO and YERVOY 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%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated hepatitis occurred in 15% (70/456) of patients, including Grade 4 (2.4%), Grade 3 (11%), and Grade 2 (1.8%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated hepatitis occurred in 7% (48/666) of patients, including Grade 4 (1.2%), Grade 3 (4.9%), and Grade 2 (0.4%).
- OPDIVO in combination with cabozantinib can cause hepatic toxicity with higher frequencies of Grade 3 and 4 ALT and AST elevations compared to OPDIVO alone. Consider more frequent monitoring of liver enzymes as compared to when the drugs are administered as single agents. In patients receiving OPDIVO and cabozantinib, Grades 3 and 4 increased ALT or AST were seen in 11% of patients.

Immune-Mediated Endocrinopathies

- OPDIVO and YERVOY 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 and YERVOY 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 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, adrenal insufficiency occurred in 8% (35/456), including Grade 4 (0.2%), Grade 3 (2.4%), and Grade 2 (4.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, adrenal insufficiency occurred in 7% (48/666) of patients, including Grade 4 (0.3%), Grade 3 (2.5%), and Grade 2 (4.1%). In patients receiving OPDIVO and cabozantinib, adrenal insufficiency occurred in 4.7% (15/320) of patients, including Grade 3 (2.2%) and Grade 2 (1.9%).

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OPDIVO® Important Safety Information (cont'd)

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

Immune-Mediated Endocrinopathies (cont'd)

- 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 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hypophysitis occurred in 9% (42/456), including Grade 3 (2.4%) and Grade 2 (6%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hypophysitis occurred in 4.4% (29/666) of patients, including Grade 4 (0.3%), Grade 3 (2.4%), and Grade 2 (0.9%).
- In patients receiving OPDIVO monotherapy, thyroiditis occurred in 0.6% (12/1994) of patients, including Grade 2 (0.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, thyroiditis occurred in 2.7% (22/666) of patients, including Grade 3 (4.5%) and Grade 2 (2.2%).
- 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 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hyperthyroidism occurred in 9% (42/456) of patients, including Grade 3 (0.9%) and Grade 2 (4.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hyperthyroidism occurred in 12% (80/666) of patients, including Grade 3 (0.6%) and Grade 2 (4.5%).
- 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 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hypothyroidism occurred in 20% (91/456) of patients, including Grade 3 (0.4%) and Grade 2 (11%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hypothyroidism occurred in 18% (122/666) of patients, including Grade 3 (0.6%) and Grade 2 (11%).
- 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. In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, diabetes occurred in 2.7% (15/666) of patients, including Grade 4 (0.6%), Grade 3 (0.3%), and Grade 2 (0.9%).

Immune-Mediated Nephritis with Renal Dysfunction

- OPDIVO and YERVOY 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%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated nephritis with renal dysfunction occurred in 4.1% (27/666) of patients, including Grade 4 (0.6%), Grade 3 (1.1%), and Grade 2 (2.2%).

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.
- YERVOY can cause immune-mediated rash or dermatitis, including bullous and exfoliative dermatitis, SJS, TEN, and DRESS. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes.
- Withhold or permanently discontinue OPDIVO and YERVOY 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%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated rash occurred in 28% (127/456) of patients, including Grade 3 (4.8%) and Grade 2 (10%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated rash occurred in 16% (108/666) of patients, including Grade 3 (3.5%) and Grade 2 (4.2%).

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 OPDIVO in combination with YERVOY 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.
- In addition to the immune-mediated adverse reactions listed above, across clinical trials of YERVOY monotherapy or in combination with OPDIVO, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1% of patients unless otherwise specified: *nervous system*: autoimmune neuropathy (2%), myasthenic syndrome/myasthenia gravis, motor dysfunction; *cardiovascular*: angiopathy, temporal arteritis; ocular: blepharitis, episcleritis, orbital myositis, scleritis; *gastrointestinal*: pancreatitis (1.3%); *other (hematologic/immune)*: conjunctivitis, cytopenias (2.5%), eosinophilia (2.1%), erythema multiforme, hypersensitivity vasculitis, neurosensory hypoacusis, psoriasis.
- 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 and YERVOY, as this may require treatment with systemic corticosteroids to reduce the risk of permanent vision loss.

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OPDIVO® Important Safety Information (cont'd)

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Infusion-Related Reactions

- OPDIVO and YERVOY can cause severe infusion-related reactions. Discontinue OPDIVO and YERVOY 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. In melanoma patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 2.5% (10/407) of patients. In HCC patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 8% (4/49) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 5.1% (28/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, infusion-related reactions occurred in 4.2% (5/119) of patients. In MPM patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, infusion-related reactions occurred in 12% (37/300) of patients.

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

Embryo-Fetal Toxicity

- Based on its mechanism of action and findings from animal studies, OPDIVO and YERVOY can cause fetal harm when administered to a pregnant woman. The effects of YERVOY are likely to be greater during the second and third trimesters of pregnancy. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO and YERVOY 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 or YERVOY 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 037, serious adverse reactions occurred in 41% of patients receiving OPDIVO (n=268). Grade 3 and 4 adverse reactions occurred in 42% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse drug reactions reported in 2% to <5% of patients receiving OPDIVO were abdominal pain, hyponatremia, increased aspartate aminotransferase, and increased lipase. In Checkmate 066, serious adverse reactions occurred in 36% of patients receiving OPDIVO (n=206). Grade 3 and 4 adverse reactions occurred in 41% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of patients receiving OPDIVO were gamma-glutamyltransferase increase (3.9%) and diarrhea (3.4%). In Checkmate 067, serious adverse reactions (74% and 44%), adverse reactions leading to permanent discontinuation (47% and 18%) or to dosing delays (58% and 36%), and Grade 3 or 4 adverse reactions (72% and 51%) all occurred more frequently in the OPDIVO plus YERVOY arm (n=313) relative to the OPDIVO arm (n=313). The most frequent (≥10%) serious adverse reactions in the OPDIVO plus YERVOY arm and the OPDIVO arm, respectively, were diarrhea (13% and 2.2%), colitis (10% and 1.9%), and pyrexia (10% and 1.0%). In Checkmate 238, serious adverse reactions occurred in 18% of patients receiving OPDIVO (n=452). Grade 3 or 4 adverse reactions occurred in 25% of OPDIVO-treated patients (n=452). The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of OPDIVO-treated patients were diarrhea and increased lipase and amylase. 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. In Checkmate 227, serious adverse reactions occurred in 58% of patients (n=576). The most frequent (≥2%) serious adverse reactions were pneumonia, diarrhea/colitis, pneumonitis, hepatitis, pulmonary embolism, adrenal insufficiency, and hypophysitis. Fatal adverse reactions occurred in 1.7% of patients; these included events of pneumonitis (4 patients), myocarditis, acute kidney injury, shock, hyperglycemia, multi-system organ failure, and renal failure. In Checkmate 9LA, serious adverse reactions occurred in 57% of patients (n=358). The most frequent (>2%) serious adverse reactions were pneumonia, diarrhea, febrile neutropenia, anemia, acute kidney injury, musculoskeletal pain, dyspnea, pneumonitis, and respiratory failure. Fatal adverse reactions occurred in 7 (2%) patients, and included hepatic toxicity, acute renal failure, sepsis, pneumonitis, diarrhea with hypokalemia, and massive hemoptysis in the setting of thrombocytopenia. In Checkmate 017 and 057, serious adverse reactions occurred in 46% of patients receiving OPDIVO (n=418). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In Checkmate 057, fatal adverse reactions occurred; these

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Serious Adverse Reactions (cont'd)

included events of infection (7 patients, including one case of *Pneumocystis jirovecii* pneumonia), pulmonary embolism (4 patients), and limbic encephalitis (1 patient). In Checkmate 743, serious adverse reactions occurred in 54% of patients receiving OPDIVO plus YERVOY. The most frequent serious adverse reactions reported in ≥2% of patients were pneumonia, pyrexia, diarrhea, pneumonitis, pleural effusion, dyspnea, acute kidney injury, infusion-related reaction, musculoskeletal pain, and pulmonary embolism. Fatal adverse reactions occurred in 4 (1.3%) patients and included pneumonitis, acute heart failure, sepsis, and encephalitis. In Checkmate 214, serious adverse reactions occurred in 59% of patients receiving OPDIVO plus YERVOY (n=547). The most frequent serious adverse reactions reported in ≥2% of patients were diarrhea, pyrexia, pneumonia, pneumonitis, hypophysitis, acute kidney injury, dyspnea, adrenal insufficiency, and colitis. In Checkmate 9ER, serious adverse reactions occurred in 48% of patients receiving OPDIVO and cabozantinib (n=320). The most frequent serious adverse reactions reported in ≥2% of patients were diarrhea, pneumonia, pneumonitis, pulmonary embolism, urinary tract infection, and hyponatremia. Fatal intestinal perforations occurred in 3 (0.9%) patients. In Checkmate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). The most frequent serious adverse reactions reported in ≥2% of patients were acute kidney injury, pleural effusion, pneumonia, diarrhea, and hypercalcemia. In Checkmate 205 and 039, adverse reactions leading to discontinuation occurred in 7% and dose delays due to adverse reactions occurred in 34% of patients (n=266). Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions reported in ≥1% of patients were pneumonia, infusion-related reaction, pyrexia, colitis or diarrhea, pleural effusion, pneumonitis, and rash. Eleven patients died from causes other than disease progression: 3 from adverse reactions within 30 days of the last OPDIVO dose, 2 from infection 8 to 9 months after completing OPDIVO, and 6 from complications of allogeneic HSCT. In Checkmate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO (n=236). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were pneumonia, dyspnea, respiratory failure, respiratory tract infection, and sepsis. In Checkmate 275, serious adverse reactions occurred in 54% of patients receiving OPDIVO (n=270). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were urinary tract infection, sepsis, diarrhea, small intestine obstruction, and general physical health deterioration. 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%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY (n=119), serious adverse reactions occurred in 47% of patients. The most frequent serious adverse reactions reported in ≥2% of patients were colitis/diarrhea, hepatic events, abdominal pain, acute kidney injury, pyrexia, and dehydration. In Checkmate 040, serious adverse reactions occurred in 59% of patients receiving OPDIVO with YERVOY (n=49). Serious adverse reactions reported in ≥4% of patients were pyrexia, diarrhea, anemia, increased AST, adrenal insufficiency, ascites, esophageal varices hemorrhage, hyponatremia, increased blood bilirubin, and pneumonitis. In Attraction-3, serious adverse reactions occurred in 38% of patients receiving OPDIVO (n=209). Serious adverse reactions reported in ≥2% of patients who received OPDIVO were pneumonia, esophageal fistula, interstitial lung disease, and pyrexia. The following fatal adverse reactions occurred in patients who received OPDIVO: interstitial lung disease or pneumonitis (1.4%), pneumonia (1.0%), septic shock (0.5%), esophageal fistula (0.5%), gastrointestinal hemorrhage (0.5%), pulmonary embolism (0.5%), and sudden death (0.5%). 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 648, serious adverse reactions occurred in 62% of patients receiving OPDIVO in combination with chemotherapy (n=310). The most frequent serious adverse reactions reported in ≥2% of patients who received OPDIVO with chemotherapy were pneumonia (11%), dysphagia (7%), esophageal stenosis (2.9%), acute kidney injury (2.9%), and pyrexia (2.3%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with chemotherapy; these included pneumonitis, pneumatosis intestinalis, pneumonia, and acute kidney injury. In Checkmate 648, serious adverse reactions occurred in 69% of patients receiving OPDIVO in combination with YERVOY (n=322). The most frequent serious adverse reactions reported in ≥2% who received OPDIVO in combination with YERVOY were pneumonia (10%), pyrexia (4.3%), pneumonitis (4.0%), aspiration pneumonia (3.7%), dysphagia (3.7%), hepatic function abnormal (2.8%), decreased appetite (2.8%), adrenal insufficiency (2.5%), and dehydration (2.5%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with YERVOY; these included pneumonitis, interstitial lung disease, pulmonary embolism, and acute respiratory distress syndrome. 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 037, the most common adverse reaction (≥20%) reported with OPDIVO (n=268) was rash (21%). In Checkmate 066, the most common adverse reactions (≥20%) reported with OPDIVO (n=206) vs dacarbazine (n=205) were fatigue (49% vs 39%), musculoskeletal pain (32% vs 25%), rash (28% vs 12%), and pruritus (23% vs 12%). In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO plus YERVOY arm (n=313) were fatigue (62%), diarrhea (54%), rash (53%), nausea (44%), pyrexia (40%), pruritus (39%), musculoskeletal pain (32%), vomiting (31%), decreased appetite (29%), cough (27%), headache (26%), dyspnea (24%), upper respiratory tract infection (23%), arthralgia (21%), and increased transaminases (25%). In Checkmate 067, the

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Common Adverse Reactions (cont'd)

most common (≥20%) adverse reactions in the OPDIVO arm (n=313) were fatigue (59%), rash (40%), musculoskeletal pain (42%), diarrhea (36%), nausea (30%), cough (28%), pruritus (27%), upper respiratory tract infection (22%), decreased appetite (22%), headache (22%), constipation (21%), arthralgia (21%), and vomiting (20%). In Checkmate 238, the most common adverse reactions (≥20%) reported in OPDIVO-treated patients (n=452) vs ipilimumab-treated patients (n=453) were fatigue (57% vs 55%), diarrhea (37% vs 55%), rash (35% vs 47%), musculoskeletal pain (32% vs 27%), pruritus (28% vs 37%), headache (23% vs 31%), nausea (23% vs 28%), upper respiratory infection (22% vs 15%), and abdominal pain (21% vs 23%). The most common immune-mediated adverse reactions were rash (16%), diarrhea/colitis (6%), and hepatitis (3%). 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%). In Checkmate 227, the most common (≥20%) adverse reactions were fatigue (44%), rash (34%), decreased appetite (31%), musculoskeletal pain (27%), diarrhea/colitis (26%), dyspnea (26%), cough (23%), hepatitis (21%), nausea (21%), and pruritus (21%). In Checkmate 9LA, the most common (>20%) adverse reactions were fatigue (49%), musculoskeletal pain (39%), nausea (32%), diarrhea (31%), rash (30%), decreased appetite (28%), constipation (21%), and pruritus (21%). In Checkmate 017 and 057, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=418) were fatigue, musculoskeletal pain, cough, dyspnea, and decreased appetite. In Checkmate 743, the most common adverse reactions (≥20%) in patients receiving OPDIVO plus YERVOY were fatigue (43%), musculoskeletal pain (38%), rash (34%), diarrhea (32%), dyspnea (27%), nausea (24%), decreased appetite (24%), cough (23%), and pruritus (21%). In Checkmate 214, the most common adverse reactions (≥20%) reported in patients treated with OPDIVO plus YERVOY (n=547) were fatigue (58%), rash (39%), diarrhea (38%), musculoskeletal pain (37%), pruritus (33%), nausea (30%), cough (28%), pyrexia (25%), arthralgia (23%), decreased appetite (21%), dyspnea (20%), and vomiting (20%). In Checkmate 9ER, the most common adverse reactions (≥20%) in patients receiving OPDIVO and cabozantinib (n=320) were diarrhea (64%), fatigue (51%), hepatotoxicity (44%), palmar-plantar erythrodysaesthesia syndrome (40%), stomatitis (37%), rash (36%), hypertension (36%), hypothyroidism (34%), musculoskeletal pain (33%), decreased appetite (28%), nausea (27%), dysgeusia (24%), abdominal pain (22%), cough (20%) and upper respiratory tract infection (20%). In Checkmate 025, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=406) vs everolimus (n=397) were fatigue (56% vs 57%), cough (34% vs 38%), nausea (28% vs 29%), rash (28% vs 36%), dyspnea (27% vs 31%), diarrhea (25% vs 32%), constipation (23% vs 18%), decreased appetite (23% vs 30%), back pain (21% vs 16%), and arthralgia (20% vs 14%). In Checkmate 205 and 039, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=266) were upper respiratory tract infection (44%), fatigue (39%), cough (36%), diarrhea (33%), pyrexia (29%), musculoskeletal pain (26%), rash (24%), nausea (20%) and pruritus (20%). In Checkmate 141, the most common adverse reactions (≥10%) in patients receiving OPDIVO (n=236) were cough (14%) and dyspnea (14%) at a higher incidence than investigator's choice. In Checkmate 275, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=270) were fatigue (46%), musculoskeletal pain (30%), nausea (22%), and decreased appetite (22%). 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 Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO as a single agent (n=74), the most common adverse reactions (≥20%) were fatigue (54%), diarrhea (43%), abdominal pain (34%), nausea (34%), vomiting (28%), musculoskeletal pain (28%), cough (26%), pyrexia (24%), rash (23%), constipation (20%), and upper respiratory tract infection (20%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY (n=119), the most common adverse reactions (≥20%) were fatigue (49%), diarrhea (45%), pyrexia (36%), musculoskeletal pain (36%), abdominal pain (30%), pruritus (28%), nausea (26%), rash (25%), decreased appetite (20%), and vomiting (20%). In Checkmate 040, the most common adverse reactions (≥20%) in patients receiving OPDIVO with YERVOY (n=49), were rash (53%), pruritus (53%), musculoskeletal pain (41%), diarrhea (39%), cough (37%), decreased appetite (35%), fatigue (27%), pyrexia (27%), abdominal pain (22%), headache (22%), nausea (20%), dizziness (20%), hypothyroidism (20%), and weight decreased (20%). In Attraction-3, the most common adverse reactions (≥20%) in OPDIVO-treated patients (n=209) were rash (22%) and decreased appetite (21%). 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 648, the most common adverse reactions (≥20%) in patients treated with OPDIVO in combination with chemotherapy (n=310) were nausea (65%), decreased appetite (51%), fatigue (47%), constipation (44%), stomatitis (44%), diarrhea (29%), and vomiting (23%). In Checkmate 648, the most common adverse reactions reported in ≥20% of patients treated with OPDIVO in combination with YERVOY were rash (31%), fatigue (28%), pyrexia (23%), nausea (22%), diarrhea (22%), and constipation (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%).

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OPDIVO® Important Safety Information (cont'd)

See Opdualag™ (nivolumab and relatlimab-rmbw) Important Safety Information on pages 29–30.

Clinical Trials and Patient Populations

Checkmate 037–previously treated metastatic melanoma
Checkmate 066–previously untreated metastatic melanoma
Checkmate 067–previously untreated metastatic melanoma, as a single agent or in combination with YERVOY®
Checkmate 238–adjuvant treatment of melanoma
Checkmate 816–neoadjuvant non-small cell lung cancer, in combination with platinum-doublet chemotherapy
Checkmate 227–previously untreated metastatic non-small cell lung cancer, in combination with YERVOY
Checkmate 9LA–previously untreated recurrent or metastatic non-small cell lung cancer in combination with YERVOY and 2 cycles of platinum-doublet chemotherapy by histology
Checkmate 017–second-line treatment of metastatic squamous non-small cell lung cancer
Checkmate 057–second-line treatment of metastatic non-squamous non-small cell lung cancer
Checkmate 743–previously untreated unresectable malignant pleural mesothelioma, in combination with YERVOY
Checkmate 214–previously untreated renal cell carcinoma, in combination with YERVOY
Checkmate 9ER–previously untreated renal cell carcinoma, in combination with cabozantinib
Checkmate 025–previously treated renal cell carcinoma
Checkmate 205/039–classical Hodgkin lymphoma
Checkmate 141–recurrent or metastatic squamous cell carcinoma of the head and neck
Checkmate 275–previously treated advanced or metastatic urothelial carcinoma
Checkmate 274–adjuvant treatment of urothelial carcinoma
Checkmate 142–MSI-H or dMMR metastatic colorectal cancer, as a single agent or in combination with YERVOY
Checkmate 040–hepatocellular carcinoma, in combination with YERVOY
Attraction-3–esophageal squamous cell carcinoma
Checkmate 577–adjuvant treatment of esophageal or gastroesophageal junction cancer
Checkmate 648–previously untreated, unresectable advanced, metastatic esophageal squamous cell carcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy;
Checkmate 648–previously untreated, unresectable advanced, or metastatic esophageal squamous cell carcinoma, in combination with YERVOY
Checkmate 649–previously untreated advanced or metastatic gastric or gastroesophageal junction or esophageal adenocarcinoma

Please see additional Important Safety Information for OPDIVO and YERVOY on pages 23–28, for Opdualag on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.
Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

Opdualag™ Important Safety Information

Severe and Fatal Immune-Mediated Adverse Reactions

- Immune-mediated adverse reactions (IMARs) listed herein may not include all possible severe and fatal immune-mediated adverse reactions.
- IMARs which may be severe or fatal, can occur in any organ system or tissue. IMARs can occur at any time after starting treatment with a LAG-3 and PD-1/PD-L1 blocking antibodies. While IMARs usually manifest during treatment, they can also occur after discontinuation of Opdualag. Early identification and management of IMARs are essential to ensure safe use. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying IMARs. Evaluate clinical chemistries including liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected IMARs, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if Opdualag requires interruption or discontinuation, 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 IMARs 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

- Opdualag can cause immune-mediated pneumonitis, which may be fatal. In patients treated with other PD-1/PD-L1 blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.7% (13/355) of patients receiving Opdualag, including Grade 3 (0.6%), and Grade 2 (2.3%) adverse reactions. Pneumonitis led to permanent discontinuation of Opdualag in 0.8% and withholding of Opdualag in 1.4% of patients.

Immune-Mediated Colitis

- Opdualag can cause immune-mediated colitis, defined as requiring use of corticosteroids and no clear alternate etiology. A common symptom included in the definition of colitis was diarrhea. Cytomegalovirus 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.
- Immune-mediated diarrhea or colitis occurred in 7% (24/355) of patients receiving Opdualag, including Grade 3 (1.1%) and Grade 2 (4.5%) adverse reactions. Colitis led to permanent discontinuation of Opdualag in 2% and withholding of Opdualag in 2.8% of patients.

Immune-Mediated Hepatitis

- Opdualag can cause immune-mediated hepatitis, defined as requiring the use of corticosteroids and no clear alternate etiology.
- Immune-mediated hepatitis occurred in 6% (20/355) of patients receiving Opdualag, including Grade 4 (0.6%), Grade 3 (3.4%), and Grade 2 (1.4%) adverse reactions. Hepatitis led to permanent discontinuation of Opdualag in 1.7% and withholding of Opdualag in 2.3% of patients.

Immune-Mediated Endocrinopathies

- Opdualag can cause primary or secondary adrenal insufficiency, hypophysitis, thyroid disorders, and Type 1 diabetes mellitus, which can be present with diabetic ketoacidosis. Withhold or permanently discontinue Opdualag 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. In patients receiving Opdualag, adrenal insufficiency occurred in 4.2% (15/355) of patients receiving Opdualag, including Grade 3 (1.4%) and Grade 2 (2.5%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of Opdualag in 1.1% and withholding of Opdualag in 0.8% of patients.
- 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. Hypophysitis occurred in 2.5% (9/355) of patients receiving Opdualag, including Grade 3 (0.3%) and Grade 2 (1.4%) adverse reactions. Hypophysitis led to permanent discontinuation of Opdualag in 0.3% and withholding of Opdualag in 0.6% of patients.
- Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism; initiate hormone replacement or medical management as clinically indicated. Thyroiditis occurred in 2.8% (10/355) of patients receiving Opdualag, including Grade 2 (1.1%) adverse reactions. Thyroiditis did not lead to permanent discontinuation of Opdualag. Thyroiditis led to withholding of Opdualag in 0.3% of patients. Hyperthyroidism occurred in 6% (22/355) of patients receiving Opdualag, including Grade 2 (1.4%) adverse reactions. Hyperthyroidism did not lead to permanent discontinuation of Opdualag. Hyperthyroidism led to withholding of Opdualag in 0.3% of patients. Hypothyroidism occurred in 17% (59/355) of patients receiving Opdualag, including Grade 2 (11%) adverse reactions. Hypothyroidism led to the permanent discontinuation of Opdualag in 0.3% and withholding of Opdualag in 2.5% of patients.
- Monitor patients for hyperglycemia or other signs and symptoms of diabetes; initiate treatment with insulin as clinically indicated. Diabetes occurred in 0.3% (1/355) of patients receiving Opdualag, a Grade 3 (0.3%) adverse reaction, and no cases of diabetic ketoacidosis. Diabetes did not lead to the permanent discontinuation or withholding of Opdualag in any patient.

Immune-Mediated Nephritis with Renal Dysfunction

- Opdualag can cause immune-mediated nephritis, which is defined as requiring use of steroids and no clear etiology. In patients receiving Opdualag, immune-mediated nephritis and renal dysfunction occurred in 2% (7/355) of patients, including Grade 3 (1.1%) and Grade 2 (0.8%) adverse reactions. Immune-mediated nephritis and renal dysfunction led to permanent discontinuation of Opdualag in 0.8% and withholding of Opdualag in 0.6% of patients.
- Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

(continued on next page)

Opdualag™ Important Safety Information (cont'd)

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

Immune-Mediated Dermatologic Adverse Reactions

- Opdualag can cause immune-mediated rash or dermatitis, defined as requiring use of steroids and no clear alternate etiology. Exfoliative dermatitis, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and Drug Rash with eosinophilia and systemic symptoms has occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.
- Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).
- Immune-mediated rash occurred in 9% (33/355) of patients, including Grade 3 (0.6%) and Grade 2 (3.4%) adverse reactions. Immune-mediated rash did not lead to permanent discontinuation of Opdualag. Immune-mediated rash led to withholding of Opdualag in 1.4% of patients.

Immune-Mediated Myocarditis

- Opdualag can cause immune-mediated myocarditis, which is defined as requiring use of steroids and no clear alternate etiology. The diagnosis of immune-mediated myocarditis requires a high index of suspicion. Patients with cardiac or cardio-pulmonary symptoms should be assessed for potential myocarditis. If myocarditis is suspected, withhold dose, promptly initiate high dose steroids (prednisone or methylprednisolone 1 to 2 mg/kg/day) and promptly arrange cardiology consultation with diagnostic workup. If clinically confirmed, permanently discontinue Opdualag for Grade 2–4 myocarditis.
- Myocarditis occurred in 1.7% (6/355) of patients receiving Opdualag, including Grade 3 (0.6%), and Grade 2 (1.1%) adverse reactions. Myocarditis led to permanent discontinuation of Opdualag in 1.7% of patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant IMARs occurred at an incidence of <1% (unless otherwise noted) in patients who received Opdualag 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*: 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. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other IMARs, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss; *Gastrointestinal*: pancreatitis including 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, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-Related Reactions

- Opdualag can cause severe infusion-related reactions. Discontinue Opdualag in patients with severe or life-threatening infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild to moderate infusion-related reactions. In patients who received Opdualag as a 60-minute intravenous infusion, infusion-related reactions occurred in 7% (23/355) of patients.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 receptor blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.
- Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 receptor blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

- Based on its mechanism of action and data from animal studies, Opdualag 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 Opdualag for at least 5 months after the last dose of Opdualag.

Lactation

- There are no data on the presence of Opdualag in human milk, the effects on the breastfed child, or the effect on milk production. Because nivolumab and relatlimab may be excreted in human milk and because of the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with Opdualag and for at least 5 months after the last dose.

Serious Adverse Reactions

- In Relativity-047, fatal adverse reaction occurred in 3 (0.8%) patients who were treated with Opdualag; these included hemophagocytic lymphohistiocytosis, acute edema of the lung, and pneumonitis. Serious adverse reactions occurred in 36% of patients treated with Opdualag. The most frequent serious adverse reactions reported in ≥1% of patients treated with Opdualag were adrenal insufficiency (1.4%), anemia (1.4%), colitis (1.4%), pneumonia (1.4%), acute myocardial infarction (1.1%), back pain (1.1%), diarrhea (1.1%), myocarditis (1.1%), and pneumonitis (1.1%).

Common Adverse Reactions and Laboratory Abnormalities

- The most common adverse reactions reported in ≥20% of the patients treated with Opdualag were musculoskeletal pain (45%), fatigue (39%), rash (28%), pruritus (25%), and diarrhea (24%).
- The most common laboratory abnormalities that occurred in ≥20% of patients treated with Opdualag were decreased hemoglobin (37%), decreased lymphocytes (32%), increased AST (30%), increased ALT (26%), and decreased sodium (24%).

Clinical Trial and Patient Populations

RELATIVITY-047-previously untreated unresectable or metastatic melanoma

Please see additional Important Safety Information for OPDIVO® (nivolumab) and YERVOY® (ipilimumab) on pages 23–28, for Opdualag on pages 29–30, and US Full Prescribing Information for OPDIVO, YERVOY, and Opdualag.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the clinical trials.

References: 1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2022. **2.** YERVOY® (ipilimumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2022. **3.** 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. *Ann Oncol.* 2018;29(11):2208-2213. **4.** 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. **5.** Opdualag™ (nivolumab and relatlimab-rmbw) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2022.

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