In the treatment of metastatic melanoma
Choose OPDIVO® (nivolumab) + YERVOY® (ipilimumab) for the chance of durable survival\(^1,2\)

OPDIVO + YERVOY: A 1L treatment option with >50% of patients alive at 5 years\(^1,2\)

**Median overall survival at 5 years, ITT population**

<table>
<thead>
<tr>
<th></th>
<th>Median OS (95% CI)</th>
<th>n</th>
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<tbody>
<tr>
<td>OPDIVO</td>
<td>28.2–58.7 mos</td>
<td>316</td>
</tr>
<tr>
<td>YERVOY</td>
<td>16.8–24.6 mos</td>
<td>315</td>
</tr>
<tr>
<td>OPDIVO + YERVOY (95% CI: 38.2 mos–NR)</td>
<td>n=314</td>
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At 5 years, 52% of OPDIVO + YERVOY patients and 44% of OPDIVO patients were alive vs 26% with YERVOY.\(^2\)

This study was not designed to compare OPDIVO + YERVOY with OPDIVO.\(^3\)

**PFS at primary analysis of 9 months\(^1\)**

- mPFS, mos (95% CI): 11.5 (8.9–16.7) with OPDIVO + YERVOY, 6.9 (4.3–9.5) with OPDIVO, and 2.9 (2.8–3.4) with YERVOY
- HR vs YERVOY (95% CI): 0.42 (0.34–0.51; P<0.0001) for OPDIVO + YERVOY, and 0.57 (0.47–0.69; P<0.0001) for OPDIVO

**Checkmate 067 study design\(^1\)**

- OPDIVO + YERVOY was evaluated in a double-blind, randomized study of previously untreated, unresectable, or metastatic melanoma. Patients were randomized (1:1) to receive OPDIVO + YERVOY (OPDIVO 1 mg/kg and YERVOY 3 mg/kg q3w for 4 doses, followed by OPDIVO monotherapy 3 mg/kg q2w*), or OPDIVO 3 mg/kg q2w, or YERVOY 3 mg/kg q3w for 4 doses plus placebo. Major efficacy outcome measures were investigator-assessed PFS and OS.

**Additional efficacy outcome measures** were confirmed ORR and DOR.

**WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS**

YERVOY can result in severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy, and evaluate clinical chemistries including liver function tests (LFTs), adrenocorticotropic hormone (ACTH) level, and thyroid function tests, at baseline and before each dose.

Permanently discontinue YERVOY and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.

**Summary of Warnings and Precautions**

- OPDIVO is associated with the following Warnings and Precautions including immune-mediated: pneumonitis, colitis, hepatitis, endocrinopathies, nephritis and renal dysfunction, skin adverse reactions, encephalitis, other adverse reactions; infusion-related reactions; 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.

**Serious Adverse Reactions**

- In Checkmate 067, serious adverse reactions (74% and 44%) 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%).

**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%).

- In a separate Phase 3 trial of YERVOY 3 mg/kg, the most common adverse reactions (≥25%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%).

*The recommended dose of OPDIVO is 1 mg/kg administered as an IV infusion over 30 minutes, followed by YERVOY 3 mg/kg administered as an IV infusion over 80 minutes on the same day, q3w for a maximum of 4 doses or until unacceptable toxicity, whichever occurs earlier. After completing 4 doses of the combination, administer OPDIVO as a single agent, either 240 mg q2w or 480 mg q4w, as an IV infusion over 30 minutes until disease progression or unacceptable toxicity. Review the Prescribing Information for YERVOY for additional information prior to initiation.\(^1\)

1L=first line; CI=confidence interval; DOR=duration of response; HR=hazard ratio; ITT=intent to treat; IV=intravenous; mPFS=median PFS; mos=months; MT=mutant; NR=not reached; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.
In the 5-year follow-up analysis

**OPDIVO® (nivolumab) + YERVOY® (ipilimumab):**

60% OS in **BRAF MT** patients at 5 years²,⁵

**Overall survival at 5 years in **BRAF MT** patients**

**SELECT IMPORTANT SAFETY INFORMATION (cont’d)**

**Immune-Mediated Pneumonitis**

- OPDIVO can cause immune-mediated pneumonitis. Fatal cases have been reported. Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis. Administer corticosteroids for Grade 2 or more severe pneumonitis. Permanently discontinue for Grade 3 or 4 and withhold until resolution for Grade 2. In patients receiving OPDIVO monotherapy, fatal cases of immune-mediated pneumonitis have occurred. Immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated pneumonitis occurred in 6% (25/407) of patients.

**Immune-Mediated Colitis**

- OPDIVO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO monotherapy for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon re-initiation of OPDIVO. When administered with YERVOY, withhold OPDIVO and YERVOY for Grade 3 and permanently discontinue for Grade 3 or 4 or recurrent colitis. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2% (58/2914) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated colitis occurred in 26% (107/407) of patients including three fatal cases.

- In a separate Phase 3 trial of YERVOY 3 mg/kg, severe, life-threatening, or fatal (diarrhea of ≥7 stools above baseline, fever, ileus, peritoneal signs; Grade 3-5) immune-mediated enterocolitis occurred in 34 (7%) patients. Across all YERVOY-treated patients in that trial (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis.

- 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. Addition of an alternative immunosuppressive agent to the corticosteroid therapy, or replacement of the corticosteroid therapy, should be considered in corticosteroid-refractory immune-mediated colitis if other causes are excluded.

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.

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² Patients were stratified by **BRAF** status at baseline³
³ OS analysis of this pre-specified subpopulation was conducted but not powered to detect a statistical differences³

**OS in **BRAF WT** patients at 5 years**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median OS, years (95% CI)</th>
<th>HR vs YERVOY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPDIVO + YERVOY</td>
<td>3.6 (26.4 mos–NR)</td>
<td>0.57 (0.45–0.73)</td>
</tr>
<tr>
<td>OPDIVO</td>
<td>2.9 (24.1–59.2 mos)</td>
<td>0.64 (0.50–0.81)</td>
</tr>
<tr>
<td>YERVOY</td>
<td>1.5 (14.1–22.7 mos)</td>
<td></td>
</tr>
</tbody>
</table>

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CI=confidence interval; HR=hazard ratio; mos=months; MT=mutant; NR=not reached; OS=overall survival; WT=wild-type.
In the 5-year follow-up analysis
OPDIVO® (nivolumab) + YERVOY® (ipilimumab):
Response analysis of \( BRAF \) MT patients\(^2,4\)

**Complete responses ORR at 5 years**

<table>
<thead>
<tr>
<th></th>
<th>(n=60/103)</th>
<th>(n=15/100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>20%</td>
<td>5%</td>
</tr>
<tr>
<td>PR</td>
<td>38%</td>
<td>10%</td>
</tr>
</tbody>
</table>

58% (n=60/103)

58% (n=60/103)

15% (n=15/100)

OPDIVO + YERVOY

(95% CI: 48–68); n=103

YERVOY

(95% CI: 9–24); n=100

**Most responding \( BRAF \) MT patients are still alive at 5 years**

90% (95% CI: 67–98)

85% (95% CI: 69–93)

90% (95% CI: 67–98)

85% (95% CI: 69–93)

**ORR in the ITT population at 5 years (95% CI)\(^4\):**

- **OPDIVO + YERVOY:** 50% (44–55); CR: 18% (n=56), PR: 32% (n=101)
- **OPDIVO:** 42% (36–47; n=132/316); CR: 16% (n=49), PR: 26% (n=83)
- **YERVOY:** 15% (11–19; n=46/315); CR: 5% (n=15), PR: 10% (n=31)

**ORR in \( BRAF \) WT patients at 5 years (95% CI)\(^4\):**

- **OPDIVO + YERVOY:** 46% (39–53; n=97/211); CR: 17% (n=35), PR: 29% (n=62)
- **OPDIVO:** 44% (37–51; n=96/218); CR: 17% (n=38), PR: 27% (n=58)
- **YERVOY:** 14% (10–20; n=31/215); CR: 5% (n=10), PR: 10% (n=21)

**ORR in the ITT population at 9-month primary analysis (95% CI)\(^4\):**

- **OPDIVO + YERVOY:** 50% (44–55); P=0.0001; CR: 9%, PR: 41%
- **OPDIVO:** 40% (34–46); P<0.0001; CR: 9%, PR: 31%
- **YERVOY:** 14% (10–18); CR: 2%, PR: 12%

*Rates are based on Kaplan-Meier estimates.\(^4\)

\(^1\)Percentages do not total 14% due to rounding.

ORR analysis not powered to detect a statistical difference between MT and WT patients.\(^3\)

**Survival by complete or partial response in \( BRAF \) WT patients\(^4\):**

- In the OPDIVO + YERVOY arm, 86% of complete responders (95% CI: 69–94) and 71% of partial responders (95% CI: 58–81) are alive at 5 years.*
- In the OPDIVO arm, 89% of complete responders (95% CI: 74–96) and 76% of partial responders (95% CI: 63–85) are alive at 5 years.*
- In the YERVOY arm, 90% of complete responders (95% CI: 47–99) and 46% of partial responders (95% CI: 24–66) are alive at 5 years.*

**Survival by complete or partial response in the ITT population\(^4\):**

- In the OPDIVO + YERVOY arm, 88% of complete responders (95% CI: 76–94) and 76% of partial responders (95% CI: 67–83) are alive at 5 years.*
- In the OPDIVO arm, 92% of complete responders (95% CI: 80–97) and 73% of partial responders (95% CI: 62–82) are alive at 5 years.*
- In the YERVOY arm, 87% of complete responders (95% CI: 56–96) and 60% of partial responders (95% CI: 41–75) are alive at 5 years.*

**SELECT IMPORTANT SAFETY INFORMATION (cont’d)**

**Immune-Mediated Hepatitis**

- OPDIVO can cause immune-mediated hepatitis. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater transaminase elevations. Withhold OPDIVO for Grade 2 and permanently discontinue OPDIVO for Grade 3 or 4.

- In a separate Phase 3 trial of YERVOY 3 mg/kg, severe, life-threatening, or fatal hepatotoxicity (AST or ALT elevations >5x the ULN or total bilirubin elevations >3x the ULN; Grade 3-5) occurred in 8 (2%) patients, with fatal hepatic failure in 0.2% and hospitalization in 0.4%.

**Immune-Mediated Neuropathies**

- In a separate Phase 3 trial of YERVOY 3 mg/kg, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported.

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.
In the 5-year follow-up analysis

**OPDIVO®** (nivolumab) + **YERVOY®** (ipilimumab): Overall survival at 5 years\(^1,2,6\)

Overall survival in the ITT population through 5 years

The study was not designed to compare OPDIVO + YERVOY with OPDIVO.\(^3\)

**Median OS at 5 years, years (95% CI):**

- **OPDIVO + YERVOY:** NR (38.2 mos–NR)
- **OPDIVO:** 3.1 (28.2–58.7 mos)
- **YERVOY:** 1.7 (16.8–24.6 mos)

**HR for OS vs YERVOY in the primary analysis at 28 months:**

- **OPDIVO + YERVOY:** 0.55 (95% CI: 0.44–0.69); \(P<0.0001\)
- **OPDIVO:** 0.63 (95% CI: 0.50–0.78); \(P<0.0001\)

**SELECT IMPORTANT SAFETY INFORMATION (cont’d)**

**Immune-Mediated Endocrinopathies**

- OPDIVO can cause immune-mediated hypophysitis, immune-mediated adrenal insufficiency, autoimmune thyroid disorders, and Type 1 diabetes mellitus. Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency, thyroid function prior to and periodically during treatment, and hyperglycemia. Administer hormone replacement as clinically indicated and corticosteroids for Grade 2 or greater hypophysitis. Withhold for Grade 2 or 3 and permanently discontinue for Grade 4 hypophysitis. Administer corticosteroids for Grade 3 or 4 adrenal insufficiency. Withhold for Grade 2 and permanently discontinue for Grade 3 or 4 adrenal insufficiency. Administer hormone-replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 hyperglycemia.

- In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, hypophysitis occurred in 9% (36/407) of patients. In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, adrenal insufficiency occurred in 5% (21/407) of patients. In patients receiving OPDIVO monotherapy, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 9% (17/1994) of patients. Hyperthyroidism occurred in 2.7% (54/1994) of patients receiving OPDIVO monotherapy. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, hyperthyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving this dose of OPDIVO with YERVOY. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, diabetes occurred in 1.5% (6/407) of patients.

- In a separate Phase 3 trial of YERVOY 3 mg/kg, severe to life-threatening immune-mediated endocrinopathies (requiring hospitalization, urgent medical intervention, or interfering with activities of daily living; Grade 3-4) occurred in 9 (1.8%) patients. All 9 patients had hypopituitarism, and some had additional concomitant endocrinopathies such as adrenal insufficiency, hypogonadism, and hyperthyroidism. Six of the 9 patients were hospitalized for severe endocrinopathies.

**Immune-Mediated Nephritis and Renal Dysfunction**

- OPDIVO can cause immune-mediated nephritis. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grades 2-4 increased serum creatinine. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 increased serum creatinine. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients.

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.
**SELECT IMPORTANT SAFETY INFORMATION (cont’d)**

**Immune-Mediated Skin Adverse Reactions and Dermatitis**
- OPDIVO can cause immune-mediated rash, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some cases with fatal outcome. Administer corticosteroids for Grade 3 or 4 rash. Withhold for Grade 3 and permanently discontinue for Grade 4 rash. For symptoms or signs of SJS or TEN, withhold OPDIVO and refer the patient for specialized care for assessment and treatment; if confirmed, permanently discontinue. In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated rash occurred in 22.6% (92/407) of patients.

- In a separate Phase 3 trial of YERVOY 3 mg/kg, severe, life-threatening, or fatal immune-mediated dermatitis (eg, Stevens-Johnson syndrome, toxic epidermal necrosis, or rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations; Grade 3-5) occurred in 13 (2.5%) patients. 1 (0.2%) patient died as a result of toxic epidermal necrosis. 1 additional patient required hospitalization for severe dermatitis.

**Immune-Mediated Encephalitis**
- OPDIVO can cause immune-mediated encephalitis. Evaluation of patients with neurologic symptoms may include, but not be limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Withhold OPDIVO in patients with new-onset moderate to severe neurologic signs or symptoms and evaluate to rule out other causes. If other etiologies are ruled out, administer corticosteroids and permanently discontinue OPDIVO for immune-mediated encephalitis. In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated rash occurred in 22.6% (92/407) of patients.

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.

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**In the treatment of metastatic melanoma**

Choose **OPDIVO® (nivolumab)** + **YERVOY® (ipilimumab)** for the chance of **durable survival**

**Durable survival**

>50% of patients in the ITT population are alive at the 5-year follow-up analysis

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Nivolumab (OPDIVO®) + Ipilimumab (YERVOY®) is recommended as a Category 1, preferred first-line systemic therapy option for metastatic or unresectable disease regardless of **BRAF** mutation status.

**BRAF** V600E/K+ patients:
**An NCCN Category 1, Preferred Regimen**

**BRAF** wild-type patients:
**An NCCN Category 1, Preferred Regimen**

Combination targeted therapy may be preferred if clinically needed for **BRAF** V600E/K+ patients with rapidly progressing disease and/or symptoms.
SELECT IMPORTANT SAFETY INFORMATION (cont’d)

Other Immune-Mediated Adverse Reactions

● Based on the severity of the adverse reaction, permanently discontinue or withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy. Across clinical trials of OPDIVO monotherapy or in combination with YERVOY, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1.0% of patients receiving OPDIVO: myocarditis, rhabdomyolysis, myositis, uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), motor dysfunction, vasculitis, aplastic anemia, pericarditis, and myasthenic syndrome.

● 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 may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Infusion-Related Reactions

● OPDIVO can cause severe infusion-related reactions, which have been reported in <1.0% of patients in clinical trials. Discontinue OPDIVO in patients with Grade 3 or 4 infusion-related reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2. 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 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.

Embryo-Fetal Toxicity

● Based on mechanism of action, OPDIVO and YERVOY can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO or 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 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

● It is not known whether OPDIVO or YERVOY is present in human milk. Because many drugs, including antibodies, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from OPDIVO or YERVOY, advise women not to breastfeed during treatment and for at least 5 months after the last dose.

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%).

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%).

● In a separate Phase 3 trial of YERVOY 3 mg/kg, the most common adverse reactions (≥5%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%).

Please see additional Important Safety Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY, throughout, and US Full Prescribing Information for OPDIVO and YERVOY.