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

Primary analysis (PD-L1 ≥1%): median OS was 17.1 months (95% CI: 15.0–20.1) with OPDIVO + YERVOY vs 14.9 months (95% CI: 12.7–16.7) with chemo (HR=0.79; 95% CI: 0.67–0.94; P=0.0066).1

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 NSCLC, with no EGFR or ALK genomic tumor aberrations.

Primary analysis: median OS was 14.1 months (95% CI: 13.2–16.2) with OPDIVO + YERVOY and chemo vs 10.7 months (95% CI: 9.5–12.5) with chemo (HR=0.69; 95% CI: 0.55–0.87; P=0.0006).1

SELECT IMPORTANT SAFETY INFORMATION

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.

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.

Please see additional Important Safety Information for OPDIVO and YERVOY throughout and US Full Prescribing Information for OPDIVO and YERVOY.
OPDIVO + YERVOY EFFICACY: OS

Checkmate 227: In a cross-histology trial for patients with mNSCLC (PD-L1 ≥1%)

Durable survival with OPDIVO® (nivolumab) + YERVOY® (ipilimumab): 29% of patients alive at 4 years\(^2\)

**OS for PD-L1 ≥1% (extended follow-up analysis)**\(^3,4\)

<table>
<thead>
<tr>
<th>Median OS</th>
<th>Primary analysis (minimum follow-up 29.3 months)</th>
<th>OPDIVO + YERVOY (n=396)</th>
<th>Chemotherapy (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>0.76 (95% CI: 0.65–0.90)</td>
<td>0.81 (95% CI: 0.68–0.96)</td>
<td></td>
</tr>
<tr>
<td>Median follow-up of 54.8 months</td>
<td>HR=0.76 (95% CI: 0.65–0.90)</td>
<td>0.81 (95% CI: 0.68–0.96)</td>
<td></td>
</tr>
</tbody>
</table>

\(^{1}\) ORR was 36% (144/396) with OPDIVO + YERVOY and 30% (120/397) with chemotherapy\(^{1,4}\)

\(^{2}\) 5.8% CR with OPDIVO + YERVOY and 1.8% with chemotherapy\(^2\)

\(^{3}\) 34% of responders to OPDIVO + YERVOY were still responding at 4 years, and 7% of chemos responders were still responding to chemo\(^3\)

**SELECT IMPORTANT SAFETY INFORMATION**

**Severe and Fatal Immune-Mediated Adverse Reactions**

**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 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.

**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.

**Immune-Mediated Hepatitis and Hepatotoxicity**

- OPDIVO and YERVOY can cause immune-mediated hepatitis.

**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 diabetes ketoacidosis. withhold OPDIVO and YERVOY depending on severity (please see section 2.13 and Administration in the accompanying Full Prescribing Information). For Grade 2 or higher adrenal insufficiency, initiate hormone replacement as clinically indicated.

Please see additional Important Safety Information for OPDIVO and YERVOY throughout and US Full Prescribing Information for OPDIVO and YERVOY.
Checkmate 9LA: For r/m NSCLC patients, regardless of PD-L1 expression and histology

**Durable survival with OPDIVO (nivolumab) + YERVOY® (ipilimumab) with limited chemo* vs chemo: 38% of ITT patients alive at 2 years**

**Overall survival (ITT)**

- **Minimal follow-up of 24.4 months.**
  - Efficacy results from the pre-specified interim analysis when 95% events were observed (87% of the planned number of events for final analysis) with an 8.1-month minimum follow-up.*
  - Median PFS at the 23.3-month minimum follow-up: 6.7 months (95% CI: 4.4–5.4) with chemo alone; HR=0.69 (95% CI: 0.56–0.87).†
  - ORR at the 6.5-month minimum follow-up: 38% (95% CI: 33–43) with OPDIVO + YERVOY with chemo and 26% (95% CI: 21–31) with chemo.
  - Median OS at the 24.4-month follow-up analysis: 15.8 months (95% CI: 13.9–19.7) with OPDIVO + YERVOY with chemo and 10.0 months (95% CI: 9.5–12.7) with chemo. HR=0.72 (95% CI: 0.61–0.86).†
  - 33% of patients enrolled had S2 disease. 68% had S1 disease.

**Study design:** Checkmate 9LA was a randomized (1:1), open-label phase 3 study of OPDIVO 360 mg q3w in combination with YERVOY 1 mg/kg q6w and 2 cycles of histology-based chemotherapy1 versus 4 cycles of platinum-doublet chemotherapy, as a first-line treatment in patients with metastatic or recurrent NSCLC regardless of histology or PD-L1 status. Key eligibility criteria included patients 18 years or older, stage IV or recurrent NSCLC, ECOG PS 0/1, and no prior systemic anticancer therapy. Patients with known EGFR mutations or ALK translocations sensitive to available targeted inhibitor therapy, unresectable brain metastases, carcinomatous meningitis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded from the study. Treatment continued until disease progression, unacceptable toxicity, or for up to 2 years. Patients were stratified by histology (SQ vs NSQ), PD-L1 (<1% vs ≥1%), and sex.

**Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in PD-L1 subgroups; therefore, results from this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroup.

- **Primary analysis at the 8.1-month minimum follow-up:** median OS was 14.1 months (95% CI: 13.2–16.2) with OPDIVO + YERVOY with chemo vs 10.7 months (95% CI: 9.5–12.5) with chemo alone; HR=0.69 (96.71% CI: 0.55–0.87); P=0.0006.6
- **At the 24.4-month minimum follow-up:** median OS for PD-L1 <1% was 17.7 (95% CI: 13.7–20.3) with OPDIVO + YERVOY with limited chemo and 9.8 months (95% CI: 7.7–18.5) with chemo; HR=0.67 (95% CI: 0.51–0.89).6
- **At the 24.4-month minimum follow-up:** median OS for PD-L1 ≥1% was 11.8 (95% CI: 13.6–22.2) with OPDIVO + YERVOY with limited chemo and 10.9 months (95% CI: 9.5–13.2) with chemo; HR=0.70 (95% CI: 0.56–0.89).6
- 23% of patients with PD-L1 <1% treated with chemotherapy were alive at 2 years* 29% of patients with PD-L1 ≥1% treated with chemotherapy were alive at 2 years.†

**Two cycles of platinum-doublet chemotherapy.**

*In the intent-to-treat population vs chemotherapy. In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemotherapy in the experimental arm, and 4 cycles in the comparator arm; NQG: paclitaxel + carboplatin (optional) perprotocol maintenance therapy in comparator arm only. SQ: paclitaxel + carboplatin.

†In Checkmate 9LA, patients in the comparator arm received 4 cycles of platinum-doublet chemotherapy; NQG: paclitaxel + carboplatin or cisplatin (optional) perprotocol maintenance therapy in the comparator arm only. SQ: paclitaxel + carboplatin.

**SELECT IMPORTANT SAFETY INFORMATION**

**Severe and Fatal Immune-Mediated Adverse Reactions**

- OPDIVO and YERVOY can cause immune-mediated nephritis. 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 OPDIVO and/or OPDIVO + YERVOY. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative 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.
- Withdrawal or permanently discontinue OPDIVO and YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).
Checkmate 227: Adverse reactions in ≥10% of patients receiving OPDIVO® (nivolumab) + YERVOY® (ipilimumab)

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>OPDIVO + YERVOY (n=576)</th>
<th>Chemo** (n=570)</th>
<th>Grades 3–4 (%)</th>
<th>All grades (%)</th>
<th>Grades 3–4 (%)</th>
<th>All grades (%)</th>
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</thead>
<tbody>
<tr>
<td>General</td>
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<tr>
<td>Pyrexia</td>
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<td>0.5</td>
<td>11</td>
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<tr>
<td>Skin and subcutaneous tissue</td>
<td></td>
<td></td>
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<tr>
<td>Rash††</td>
<td>34</td>
<td>4.7</td>
<td>10</td>
<td>0.4</td>
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<tr>
<td>Metabolism and nutrition</td>
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<tr>
<td>Decreased appetite</td>
<td>31</td>
<td>2.3</td>
<td>26</td>
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<tr>
<td>Musculoskeletal and connective tissue</td>
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<tr>
<td>Musculoskeletal pain</td>
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<tr>
<td>Diarrhea/colitis/Constipation</td>
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<td>16</td>
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<td>Respiratory, thoracic, and mediastinal</td>
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<tr>
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<td>16</td>
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<tr>
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<tr>
<td>Hepatitis†</td>
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<td>9</td>
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<tr>
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<td>8</td>
<td>4.0</td>
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<tr>
<td>Nervous system</td>
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</tr>
<tr>
<td>Headache</td>
<td>11</td>
<td>0.5</td>
<td>6</td>
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</table>

Safety was assessed in the overall population in Checkmate 227 Part 1. Efficacy analysis was conducted in the Part 1a population.

*Includes fatigue and asthenia
†Includes pyrexia, edema, face edema, generalized edema, localized edema, edema, edema peripheral, and peripheral edema.
‡Includes autonomic dematitits, dermatitis, dermatitis acneform, dermatitis atopic, dermatitis atopic, dermatitis contact, dermatitis flexural, dermatitis folliculitis, granulomatous dermatitis, rash, pityriasis, psoriasis, drug eruption, pruritis, psoriasiform eczema, psoriasis, rival rash, rash, rash erythematous, rash generalized, rash mucosal, rash maculopapular, rash papular, rash pruritic, rash pustular, and toxic skin eruption.
§Includes pruritus and pruritis generalized.
¶Includes back pain, bone pain, muscular skeletal chest pain, musculoskeletal chest discomfort, musculoskeletal pain, myalgia, and pain in extremity.
††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡Includes alanine aminotransferase increased, aspartate aminotransferase increased, autoimmune hepatitis, blood bilirubin increased, hepatic enzyme increased, jaundice, transaminases increased, and transaminases decreased.
§§Includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, and abdominal tenderness.
¶¶Includes dyspnea and dyspnea exertional.
¶¶¶Includes cough and productive cough.
**Includes abdominal pain, abdominal pain lower, abdominal pain upper, and abdominal tenderness.
†††Includes abdominal discomfort, abdominal pain, and abdominal pain.
‡‡‡Includes abdominal pain, liver test abnormal, liver function test increased, and transaminases increased.
****Includes abdominal pain, abdominal pain, and abdominal pain.
††††Includes abdominal discomfort, abdominal pain, and abdominal pain.
†††††Includes abdominal pain, abdominal pain, and abdominal pain.
‡‡‡‡Includes abdominal pain, abdominal pain, and abdominal pain.
††††††Includes abdominal pain, abdominal pain, and abdominal pain.
‡‡‡‡‡Includes abdominal pain, abdominal pain, and abdominal pain.
†††††††Includes abdominal pain, abdominal pain, and abdominal pain.
‡‡‡‡‡‡Includes abdominal pain, abdominal pain, and abdominal pain.

Checkmate 9LA: Adverse reactions in >10% of patients receiving OPDIVO + YERVOY with limited chemo

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>OPDIVO + YERVOY with limited chemo (n=538)</th>
<th>Chemo (n=349)</th>
<th>Grades 3–4 (%)</th>
<th>All grades (%)</th>
<th>Grades 3–4 (%)</th>
<th>All grades (%)</th>
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</thead>
<tbody>
<tr>
<td>General</td>
<td></td>
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<tr>
<td>Fatigue*</td>
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<td>40</td>
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<td>Musculoskeletal and connective tissue</td>
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<td>Gastrointestinal</td>
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<td>Nausea</td>
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<td>Rash†</td>
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<td>Metabolism and nutrition</td>
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<td>2.0</td>
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<tr>
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</table>

Toxicity was graded per NCI CTCAE v4.

*Includes pyrexia and fatigue.
†Includes fever, myalgia, and non-fever.
‡Includes rash and toxic skin eruption.
§Includes rash and toxic skin eruption.
¶Includes diffuse pruritus.
||Includes rash and toxic skin eruption.
§§Includes rash and toxic skin eruption.
††Includes rash and toxic skin eruption.
‡‡Includes rash and toxic skin eruption.
†††Includes rash and toxic skin eruption.
‡‡‡Includes rash and toxic skin eruption.
††††Includes rash and toxic skin eruption.
‡‡‡‡Includes rash and toxic skin eruption.
†††††Includes rash and toxic skin eruption.
‡‡‡‡‡Includes rash and toxic skin eruption.
††††††Includes rash and toxic skin eruption.
‡‡‡‡‡‡Includes rash and toxic skin eruption.

**Includes cough, productive cough, and upper-airway cough syndrome.
††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡Includes cough, productive cough, and upper-airway cough syndrome.
†††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡‡Includes cough, productive cough, and upper-airway cough syndrome.
††††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡‡‡Includes cough, productive cough, and upper-airway cough syndrome.
†††††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡‡‡‡Includes cough, productive cough, and upper-airway cough syndrome.
††††††Includes cough, productive cough, and upper-airway cough syndrome.
‡‡‡‡‡‡Includes cough, productive cough, and upper-airway cough syndrome.
†††††††Includes cough, productive cough, and upper-airway cough syndrome.

Checkmate 227: Adverse reactions in ≥10% of patients receiving OPDIVO® and YERVOY® throughout and US Full Prescribing Information

- OPDIVO® and YERVOY® was discontinued in 24% of patients due to adverse reactions, and 53% had at least one dose withheld for an adverse reaction.
- Serious adverse reactions occurred in 58% of patients receiving OPDIVO® + YERVOY®.
- The most frequent (≥2%) serious adverse reactions were pneumonia, diabetes, pleural effusion, pyrexia, vomiting, and pyrexia.
- The most common (≥2%) adverse reactions were fatigue, rash, decreased appetite, musculoskeletal pain, diarrhea, dyspnea, abdominal pain, and pyrexia.
- Median number of doses was 9 OPDIVO® and 3 YERVOY®.
- With a minimum follow-up of 23.3 months, no new safety signals were identified for OPDIVO + YERVOY.

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


**SELECT IMPORTANT SAFETY INFORMATION**

**Severe and Fatal Immune-Mediated Adverse Reactions**

- The most common severe immune-mediated adverse reactions include: pneumonia, colitis, hepatitis, colitis, pneumonitis, and rash.
- Other immune-mediated adverse reactions include: hypophysitis, hypoadrenalism, hypothyroidism, and hyperglycemia.

**Infusion-Related Reactions**

- Infusion-related reactions are reported in patients who receive OPDIVO or YERVOY. 
- Infusion-related reactions are managed with dose reductions, discontinuation of treatment, and supportive care.

**Other Immune-Mediated Adverse Reactions**

- The most common immune-mediated adverse reactions include: rash, fatigue, and diarrhea.
- Other immune-mediated adverse reactions include: pneumonitis, colitis, and hepatitis.

**Other Adverse Reactions**

- The most common adverse reactions reported in patients who receive OPDIVO or YERVOY include: fatigue, dyspnea, and rash.
- Other adverse reactions include: nausea, vomiting, diarrhea, and constipation.

**Please see US Full Prescribing Information for OPDIVO and YERVY**
Give patients a CHANCE TO LIVE LONGER*: Durable survival with OPDIVO® (nivolumab) + YERVOY® (ipilimumab)–based combinations1

**OPDIVO + YERVOY**
- **Primary analysis** at 29.3 months minimum follow-up: median OS was 17.1 months with OPDIVO + YERVOY vs 14.9 months with chemo; HR=0.79 (95% CI: 0.67–0.94); P=0.00661,3
- ORR: 36% (144/396, 95% CI: 32–41) CR=5.8%, PR=30.1% with OPDIVO + YERVOY and 30% (120/397, 95% CI: 26–35) CR=1.8%, PR=28.2% with chemo1,4,5
- In Checkmate 227 Part 1a, PFS, ORR, and DOR were pre-specified descriptive analyses. The primary efficacy outcome measure was OS1,4
- Median TTR was 2.0 months with OPDIVO + YERVOY and 1.6 months with chemo4
- 29% of patients enrolled had SQ disease; 71% had NSQ disease1

**OPDIVO + YERVOY with limited chemo‡**
- **Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in PD-L1 subgroups; therefore, results from this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroup.
- **Primary analysis** from pre-specified interim analysis at 8.1 months minimum follow-up: median OS was 14.1 months (95% CI: 13.2–16.2) with OPDIVO + YERVOY with chemo vs 10.7 (95% CI: 9.5–12.5) with chemo; HR=0.69 (95% CI: 0.55–0.87); P=0.00061,10
- Efficacy results from the pre-specified interim when 351 events were observed (87% of the planned number of events for final analysis) with an 8.1-month minimum follow-up1,7
- Median OS at the 24.4-month minimum follow-up analysis: 15.8 months (95% CI: 13.9–19.7) with OPDIVO + YERVOY with chemo and 11.0 months (95% CI: 9.5–12.7) with chemo; HR=0.72 (95% CI: 0.61–0.86)6
- At the 24.4-month minimum follow-up, median OS for PD-L1 <1% was 17.7 (95% CI: 13.7–20.3) with OPDIVO + YERVOY with limited chemo and 9.8 months (95% CI: 7.7–13.5) with chemo; HR=0.67 (95% CI: 0.51–0.88)6
- At the 24.4-month minimum follow-up, median OS for PD-L1 ≥1% was 15.8 (95% CI: 13.8–22.2) with OPDIVO + YERVOY with limited chemo and 10.9 months (95% CI: 9.5–13.2) with chemo; HR=0.70 (95% CI: 0.56–0.89)6

*Vs chemo. In Checkmate 227, patients in the comparator arm received up to 4 cycles of platinum-doublet chemo q3w; NSQ: pemetrexed + carboplatin or cisplatin, with optional pemetrexed maintenance therapy; SQ: gemcitabine + carboplatin or cisplatin. In Checkmate 9LA, patients in the comparator arm received 4 cycles of platinum-doublet chemo q3w; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.1,2,6 †In those who responded. ‡Two cycles of platinum-doublet chemotherapy.1

**SELECT IMPORTANT SAFETY INFORMATION**

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.

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