oncology exchange
fall 2024

# Dr. Ronan Kelly

**Medical Oncologist, Baylor University Medical Center**
**The Charles A Sammons Cancer Center**

cencora

# Exploring the latest data on treatment options for patients with PD-L1 <1% metastatic and resectable non-metastatic NSCLC[1]

## 1L mNSCLC


**and 2 CYCLES OF CHEMO***

**Checkmate 9LA**

***5-YEAR DATA UPDATE***

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.

## Resectable NSCLC


**Checkmate 77T**

***2.5-YEAR DATA UPDATE***

OPDIVO®, in combination with platinum-doublet chemotherapy, is indicated for neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, followed by single-agent OPDIVO® as adjuvant treatment after surgery.

***In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed and carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel and carboplatin.[1] †Platinum-doublet chemo q3w for 3 cycles: NSQ: pemetrexed and cisplatin or carboplatin, or paclitaxel and carboplatin; SQ: docetaxel and cisplatin or paclitaxel and carboplatin.[1]

1L=first line; ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; mNSCLC=metastatic NSCLC; NSCLC=non-small cell lung cancer; NSQ=non-squamous; PD-L1=programmed death ligand 1; q3w=every 3 weeks; SQ=squamous.



Please see Important Safety Information for OPDIVO® (nivolumab) and YERVOY® (ipilimumab) at the end of the presentation and US Full Prescribing Information for OPDIVO and YERVOY provided at this presentation.

7356-US-2400503 10/24

# Select Important Safety Information

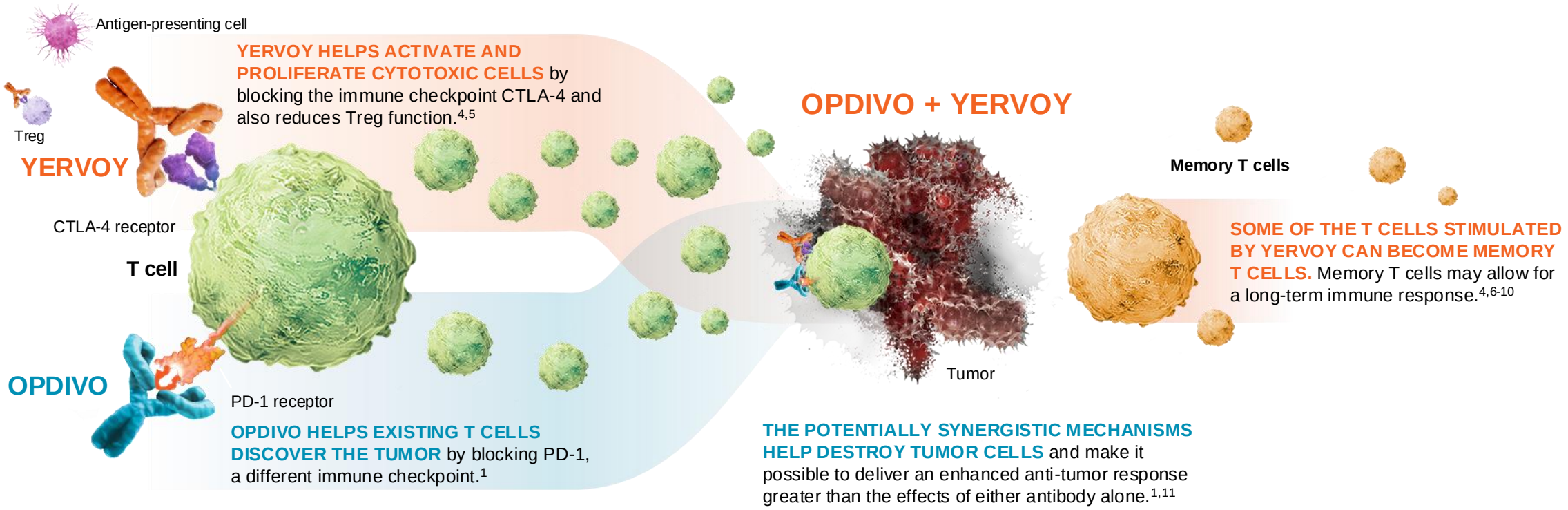
## Summary of Warnings and Precautions

OPDIVO® (nivolumab) and YERVOY® (ipilimumab) are associated with the following Warnings and Precautions: severe and fatal 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.

- Immune-mediated adverse reactions (IMAR), which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis and hepatotoxicity, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, and immune-mediated nephritis with renal dysfunction can occur at any time during treatment or after discontinuation. Monitor for early identification and management. Evaluate liver enzymes, creatinine, adrenocorticotropic hormone level, and thyroid function at baseline and periodically during treatment for OPDIVO, and before each dose for YERVOY. Withhold or permanently discontinue based on severity and type of reaction.
- Infusion-related reactions: Discontinue OPDIVO and YERVOY in patients with severe or life-threatening infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild or moderate infusion-related reactions.
- Complications of allogeneic HSCT: Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with OPDIVO or YERVOY.
- Embryo-fetal toxicity: OPDIVO and YERVOY can cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception.
- Increased mortality in patients with multiple myeloma when OPDIVO is added to a thalidomide analogue and dexamethasone: 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.

# OPDIVO® (nivolumab) + YERVOY® (ipilimumab): harnessing the immune system to help destroy tumor cells and to defend with memory[1-14]

## Targeting of normal cells can also occur.[2,3]




## CTLA-4 blockade may help lead to increase in tumor PD-L1.[12-14]*

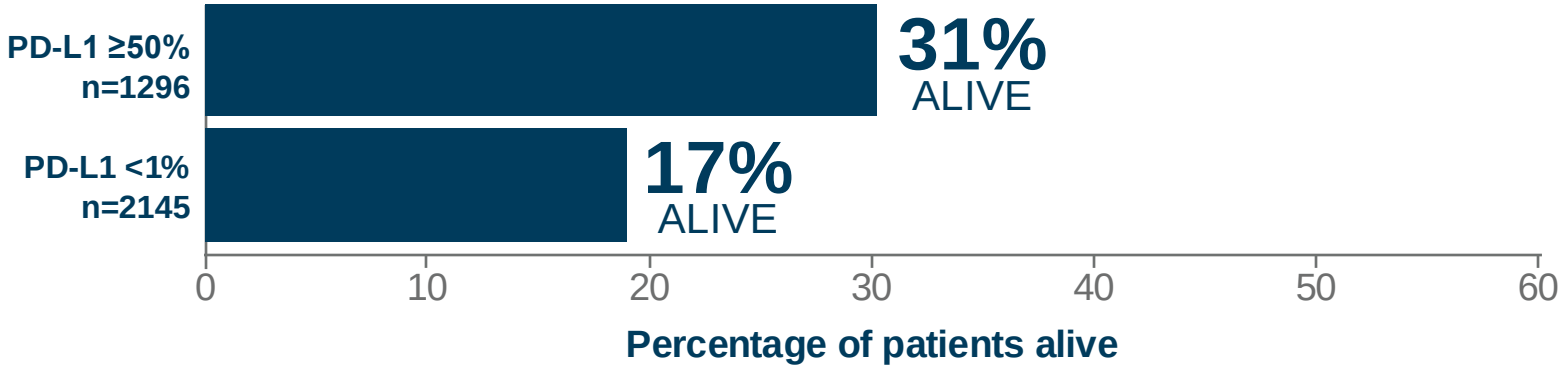
This graphic is for demonstration purposes only.
The illustrated mechanisms may vary for each patient and may not directly correlate with clinical significance.

*The actual mechanism of this effect is unclear. This is an assumption based on limited data related to the mechanistic blockade of CTLA-4 and was not specific to YERVOY.[12-14]

CTLA-4=cytotoxic T-lymphocyte antigen 4; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; T cell=cytotoxic T cell; Treg=regulatory T cell.

# Current standards of care in r/m NSCLC result in worse outcomes for patients with PD-L1 <1% compared with PD-L1 ≥50%[15]

## 3-year OS rates: Real-world anti–PD-(L)1 + chemo in patients with r/m NSCLC[15]




**In this retrospective, real-world study, ~99% (n=4218/4271) of patients were on pembrolizumab + chemo. The remaining ~1% (n=53/4271) of patients were on atezolizumab + chemo ± bevacizumab[16]**

**Limitation:** Retrospective, real-world, observational analyses are not intended for direct comparison with clinical trials. Causality cannot be established based on this dataset, as no statistical testing was performed. OPDIVO® (nivolumab) + YERVOY® (ipilimumab) regimens were not included in this analysis due to their recent approvals.

- Using current algorithms, PD-L1 <1% is detected in approximately 1/3 of patients diagnosed with mNSCLC[17]
- The median overall survival for patients with PD-L1 <1% treated with single-agent I-O + chemotherapy is 8.7–10.2 months[16]
- **Study design:** This retrospective study evaluated the clinical outcomes of real-world adult patients with confirmed stage III–IV NSCLC who received either 1L I-O monotherapy (n=3041) or single-agent I-O combined with chemotherapy (n=4271) on or after January 1, 2016. Patient data were abstracted from electronic health records in the Flatiron Health oncology database with a data cut-off date of June 30, 2020. Patients were grouped by treatment (I-O + chemo or I-O monotherapy) and stratified by histology. Patients were excluded if they had <2 documented visits on or after initial NSCLC diagnosis, *EGFR*-/*ALK*-positive tumors, or tumors with unknown histology. The primary objective was to examine OS. Secondary objectives were to evaluate duration of therapy and real-world time to progression while on treatment[16]

1L=first line; ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; I-O=immuno-oncology; mNSCLC=metastatic NSCLC; NSCLC=non-small cell lung cancer; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; OS=overall survival; r/m=recurrent or metastatic.

# Patient case*

Mary
Age: 60

## Meet Mary, newly diagnosed with mNSCLC, expressing PD-L1 <1%

Mary is a 60-year-old retired teacher who quit smoking due to chronic obstructive pulmonary disease (COPD).

She visited her doctor recently with some concerning symptoms, such as shortness of breath, cough, and fatigue. She has not previously been treated for cancer.

## Key patient information

### Biomarkers

- **PD-L1 expression: <1%**
- Negative for *EGFR, ALK, BRAF, KRAS, METex14, RET, ERBB2 (HER2), ROS1* rearrangement, and *NTRK1/2/3* fusion

### Performance status

- ECOG PS: 1

### Imaging/MRI

- Lesion in upper lobe of the right lung (7.5 cm)
- No brain metastases found

**What would you recommend as an appropriate treatment option for Mary?**

Initial diagnosis ▶ 3 bone metastases found in ribs | Stage IV SQ NSCLC

*Hypothetical patient case.

ALK=anaplastic lymphoma kinase; BRAF=V-raf murine sarcoma viral oncogene homolog B; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; HER2=human epidermal growth factor receptor 2; KRAS=Kirsten rat sarcoma; METex14=mesynchymal epithelial transition exon 14; mNSCLC=metastatic NSCLC; MRI=magnetic resonance imaging; NSCLC=non-small cell lung cancer; NTRK=neurotrophic tyrosine receptor kinase; PD-L1=programmed death ligand 1; ROS1=ROS proto oncogene 1, receptor tyrosine kinase; RET=rearranged during transfection proto oncogene, receptor tyrosine kinase; SQ=squamous.

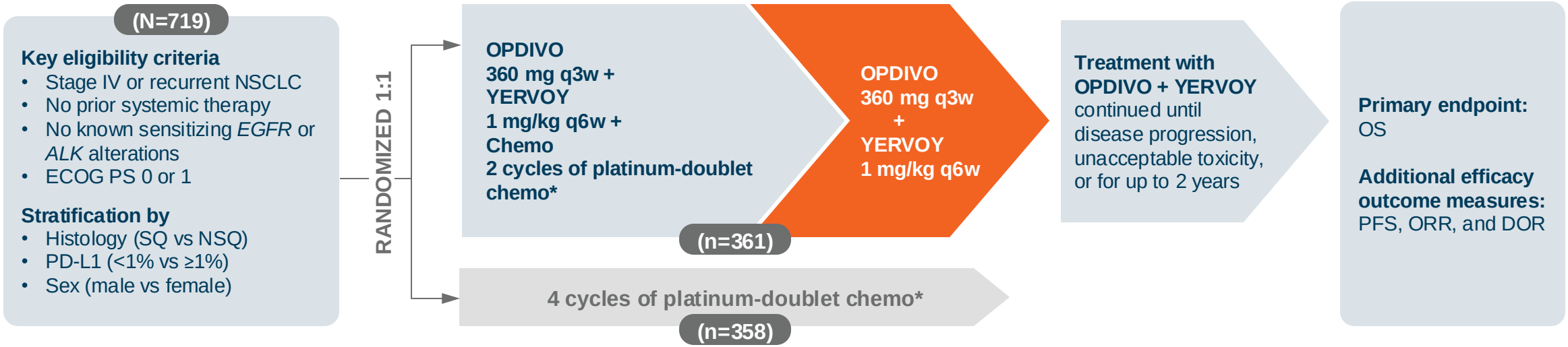
# Discussion questions

- Q Are you satisfied with your current outcomes for patients with PD-L1 <1%?
- Q What treatment option(s) would you consider for Mary, and what are your expectations for this treatment?

NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1.

# Checkmate 9LA evaluated OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo for patients with 1L r/m NSCLC regardless of PD-L1 expression and histology[1,18]

## Checkmate 9LA study design[1,18]



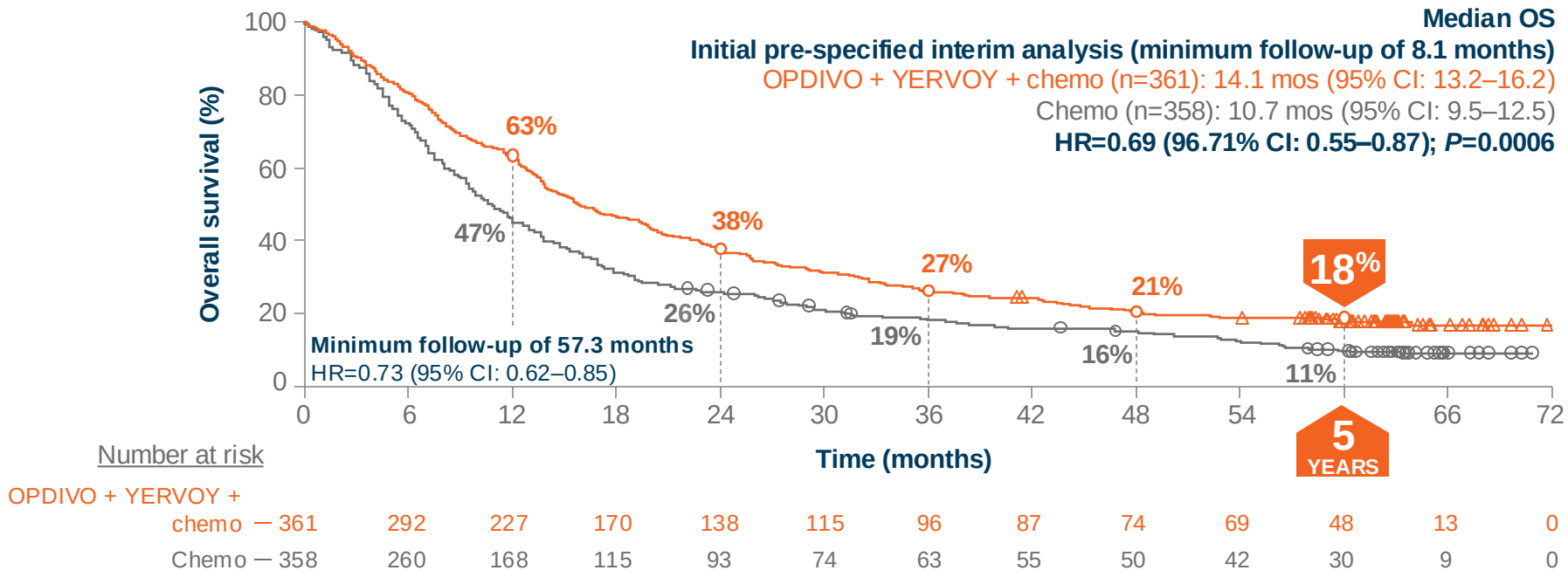

- Patients with untreated brain metastases, carcinomatous meningitis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded[1]
- Median number of doses was 9 for OPDIVO, 4 for YERVOY, and 2 cycles of chemo[19]

*In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.[1]

1L=first line; ALK=anaplastic lymphoma kinase; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; NSCLC=non-small cell lung cancer; NSQ=non-squamous; ORR=overall response rate; OS=overall survival; PD-L1=programmed death ligand 1; PFS=progression-free survival; q3w=every 3 weeks; q6w=every 6 weeks; r/m=recurrent or metastatic; SQ=squamous.

# Early separation observed* and durable survival with OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo vs chemo[1,20,21†‡]

## OS in ITT population: Extended follow-up analysis at 5 years[1,20,21]




- Efficacy results from the pre-specified interim analysis, when 351 events were observed (87% of the planned number of events for final analysis) with an 8.1-month minimum follow-up, are presented[1,21]
- With a minimum follow-up of 57.3 months, median OS was 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=0.73 (95% CI: 0.62–0.85)[20]

Minimum/median follow-up for OS: 57.3/64.5 months.[20]

**Patient cases with oncogenic mutations**

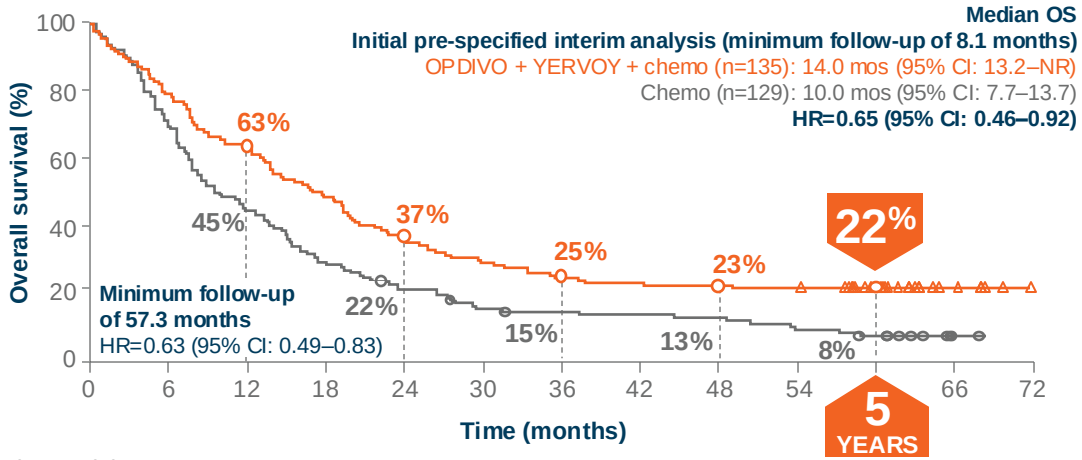
**OS data by oncogenic mutation status**

*Early separation of the curves is observational and not powered to detect differences in the treatment effect.[21] †In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in the comparator arm only); SQ: paclitaxel + carboplatin.[1] ‡In the intent-to-treat population vs chemo.[1]

CI=confidence interval; HR=hazard ratio; mo=month; ITT=intent to treat; NSCLC=non-small cell lung cancer; NSQ=non-squamous; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# Consistent, durable OS across PD-L1 <1% and PD-L1 ≥1% at 5 years with OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo vs chemo[1,20*]

## OS in PD-L1 <1%: Extended follow-up analysis at 5 years[20-22]

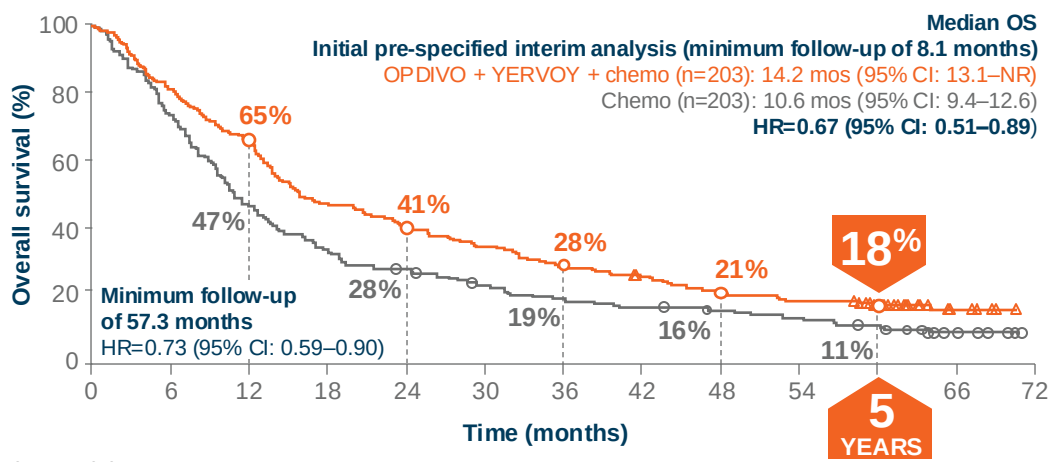



Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 135 | 107 | 85 | 66 | 50 | 40 | 34 | 32 | 31 | 30 | 22 | 6 | 0 |
| Chemo | 129 | 90 | 58 | 37 | 27 | 19 | 17 | 16 | 15 | 11 | 8 | 1 | 0 |

- At the 57.3-month minimum follow-up, median OS for PD-L1 <1% was 17.7 months (95% CI: 13.7–20.3) with OPDIVO + YERVOY with chemo and 9.8 months (95% CI: 7.7–13.5) with chemo; HR=0.63 (95% CI: 0.49–0.83)[20]

## OS in PD-L1 ≥1%: Extended follow-up analysis at 5 years[20-22]




Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 204 | 166 | 133 | 97 | 83 | 71 | 58 | 51 | 41 | 37 | 25 | 7 | 0 |
| Chemo | 204 | 151 | 96 | 68 | 56 | 45 | 37 | 33 | 29 | 25 | 19 | 8 | 0 |

- At the 57.3-month minimum follow-up, median OS for PD-L1 ≥1% was 15.8 months (95% CI: 13.8–22.2) with OPDIVO + YERVOY with chemo and 10.9 months (95% CI: 9.5–13.2) with chemo; HR=0.73 (95% CI: 0.59–0.90)[20]

**Nearly 3x the OS rate vs chemo at 5 years in patients with PD-L1 <1%[20]**

Minimum/median follow-up for OS: 57.3/64.5 months.[20]

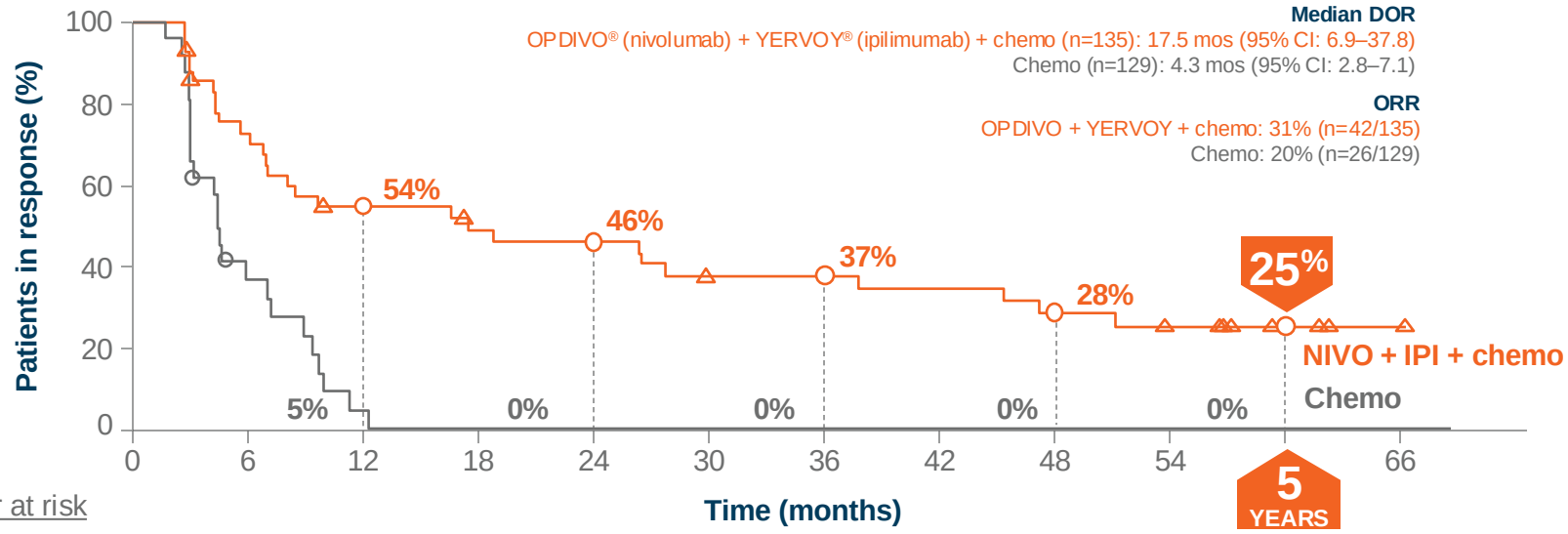
**Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in these subgroups; therefore, results from these exploratory analyses should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the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

*In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.[1]

CI=confidence interval; HR=hazard ratio; mo=month; NR=not reached; NSCLC=non-small cell lung cancer; NSQ=non-squamous; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# 25% of patients with PD-L1 <1% were still in response at 5 years[20]*†‡

## Duration of response in PD-L1 <1%: extended follow-up analysis at 5 years[20]




Number at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 42 | 28 | 20 | 17 | 16 | 12 | 12 | 11 | 9 | 7 | 3 | 1 |
| Chemo | 26 | 8 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

**In the ITT population**

- With a minimum follow-up of 57.3 months, 19% of patients were still in response in the OPDIVO + YERVOY + chemo arm (median DOR of 12.4 months [95% CI: 8.7–20.2]) compared with 8% in the chemo arm (median DOR of 5.6 months 95% CI: 4.4–7.1])[20]
- With a minimum follow-up of 57.3 months, ORR was 38% (95% CI: 33–43) with OPDIVO + YERVOY + chemo and 25% (95% CI: 21–30) with chemo[20]

**In the PD-L1 ≥1% population**

- With a minimum follow-up of 57.3 months, mDOR was 11.8 months (95% CI: 8.6–20.3) with OPDIVO + YERVOY + chemo and 5.6 months (95% CI: 4.3–8.0) with chemo[20]
- With a minimum follow-up of 57.3 months, ORR was 43% with OPDIVO + YERVOY + chemo and 28% with chemo[20]

## Most patients were off protocol therapy for ≥3 years[20§]

Minimum/median follow-up for OS: 57.3/64.5 months.[20]

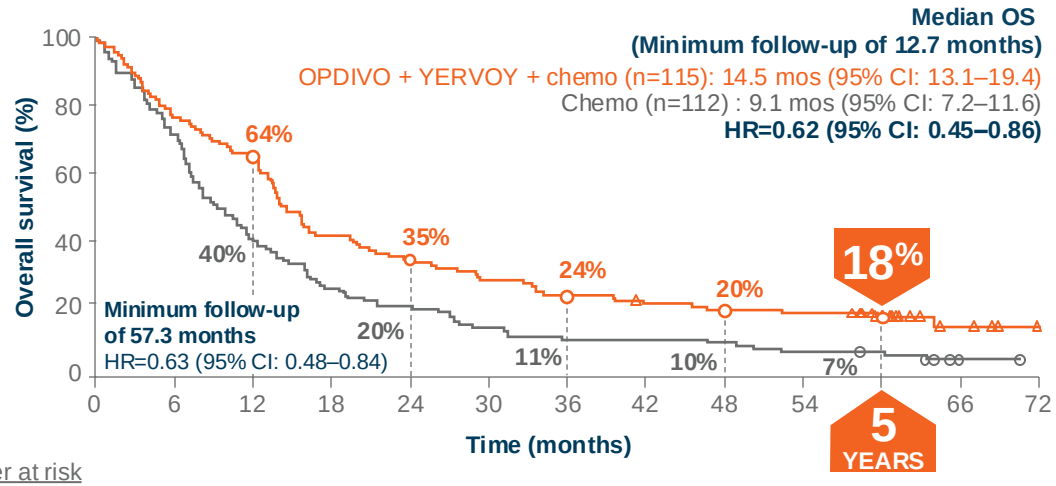
**Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in these subgroups; therefore, results from these exploratory analyses should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the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

*Post hoc exploratory analysis.[23] †In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.[1] ‡In Checkmate 9LA, the primary efficacy outcome measure was OS. Additional efficacy outcome measures included ORR and DOR.[20] §17% vs 50% of patients in the OPDIVO + YERVOY + chemo and chemo arms, respectively, received subsequent therapy.[20]

CI=confidence interval; ITT=intent to treat; DOR=duration of response; mDOR=median duration of response; mo=month; NSCLC=non-small cell lung cancer; NSQ=non-squamous; ORR=overall response rate; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# OS in patients with SQ and NSQ histology with OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo at 5 years[18,20]

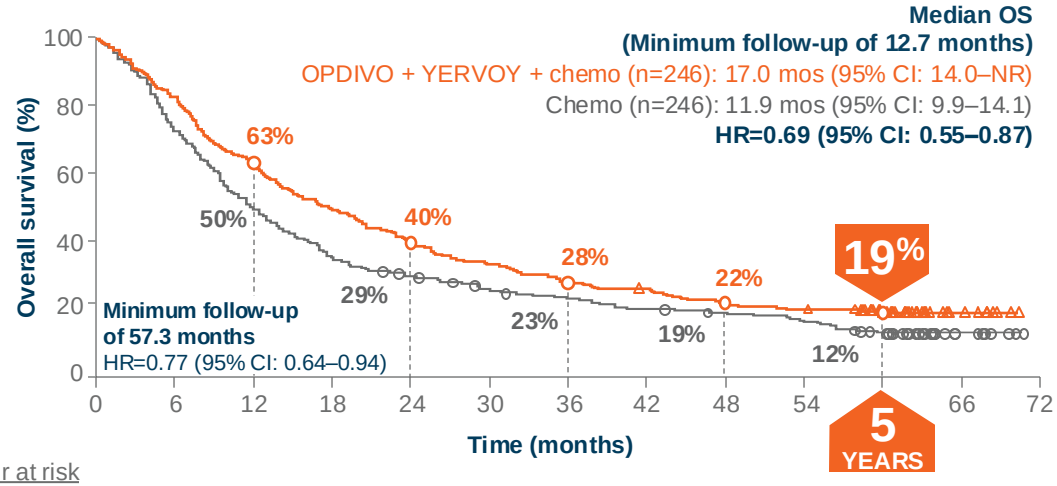
## OS in patients with SQ histology: Extended follow-up analysis at 5 years[18,20]*




Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 115 | 88 | 73 | 48 | 40 | 33 | 28 | 24 | 22 | 21 | 13 | 4 | 0 |
| Chemo | 112 | 80 | 45 | 29 | 23 | 16 | 12 | 12 | 11 | 8 | 7 | 2 | 0 |

## OS in patients with NSQ histology: Extended follow-up analysis at 5 years[18,20]*




Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 246 | 204 | 154 | 122 | 98 | 82 | 68 | 63 | 52 | 48 | 35 | 9 | 0 |
| Chemo | 246 | 180 | 123 | 86 | 70 | 58 | 51 | 43 | 39 | 34 | 23 | 7 | 0 |

- At the 57.3-month minimum follow-up, median OS for patients with SQ histology was 14.5 months (95% CI: 13.1–19.3) with OPDIVO + YERVOY with chemo and 9.1 months (95% CI: 7.2–11.6) with chemo; HR=0.63 (95% CI: 0.48–0.84)[20]

- At the 57.3-month minimum follow-up, median OS for patients with NSQ histology was 17.8 months (95% CI: 14.1–20.7) with OPDIVO + YERVOY with chemo and 12.0 months (95% CI: 9.9–13.9) with chemo; HR=0.77 (95% CI: 0.64–0.94)[20]

Minimum/median follow-up for OS: 57.3/64.5 months.[20]

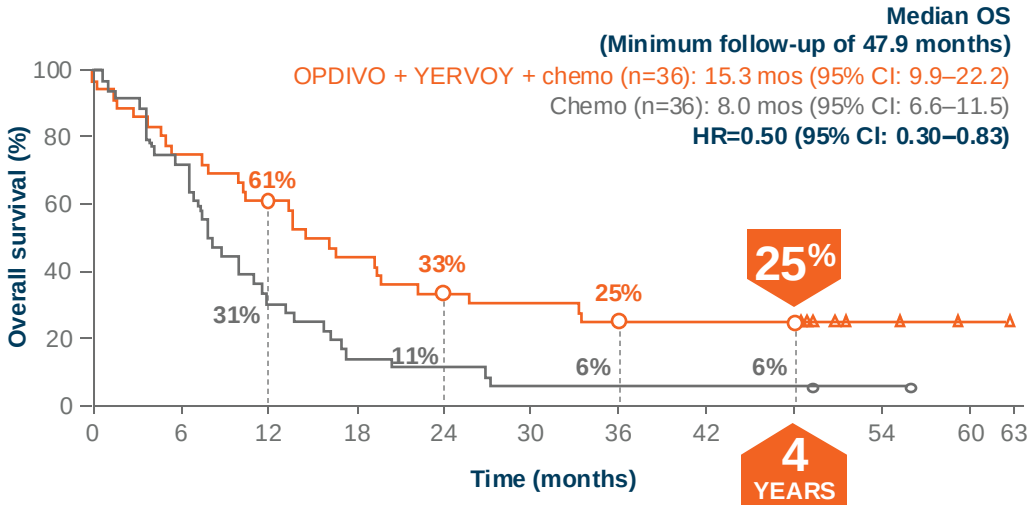
**Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in these subgroups; therefore, results from these exploratory analyses should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the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

*Post hoc exploratory analysis. In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.[1,23]

CI=confidence interval; HR=hazard ratio; mo=month; NR=not reached; NSCLC=non-small cell lung cancer; NSQ=non-squamous; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# OS by histology in patients with PD-L1 <1%, with OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo at 4 years[1,23]

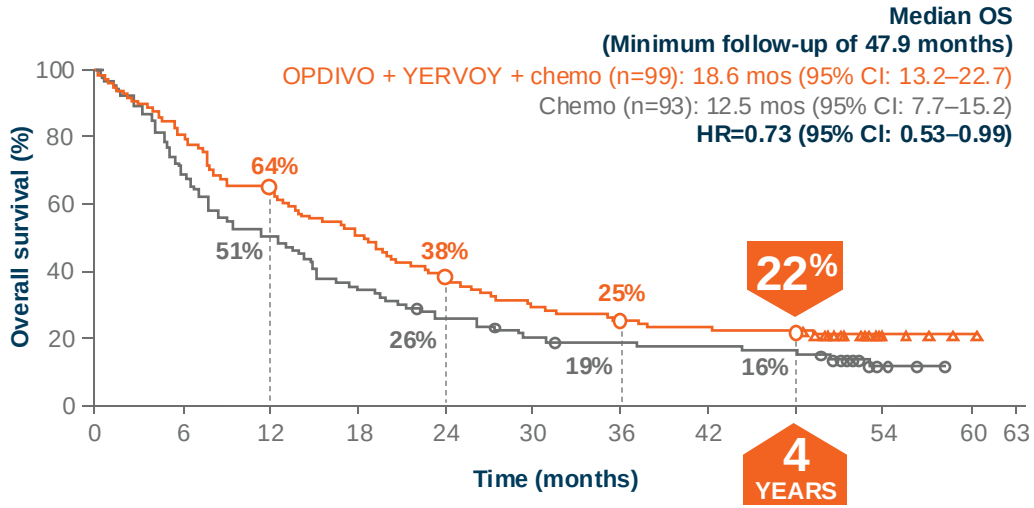
## OS in patients with PD-L1 <1% with SQ histology: Extended follow-up analysis at 4 years[23]*




Number at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 36 | 27 | 22 | 16 | 12 | 11 | 9 | 9 | 9 | 3 | 1 | 0 |
| Chemo | 36 | 26 | 11 | 5 | 4 | 2 | 2 | 2 | 2 | 1 | 0 | 0 |

## OS in patients with PD-L1 <1% with NSQ histology: Extended follow-up analysis at 4 years[23]*




Number at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 99 | 80 | 63 | 50 | 38 | 29 | 25 | 23 | 22 | 5 | 1 | 0 |
| Chemo | 93 | 64 | 47 | 32 | 23 | 17 | 15 | 14 | 13 | 3 | 0 | 0 |

Minimum/median follow-up for OS: 47.9/54.5 months.[23]

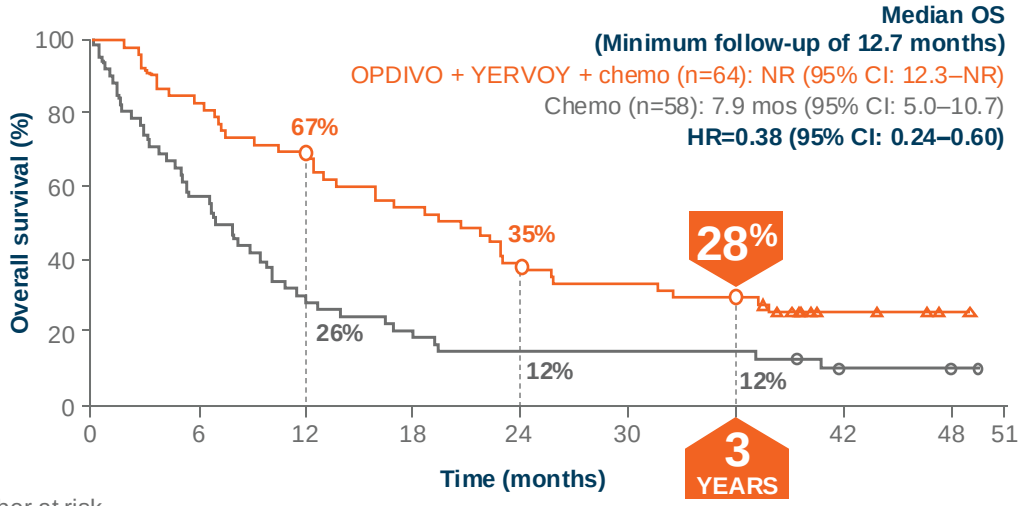
**Limitation:** Checkmate 9LA was not powered to detect differences in the treatment effect in these subgroups; therefore, results from these exploratory analyses should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the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

*Post hoc exploratory analysis. In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin.[1,23]

CI=confidence interval; HR=hazard ratio; mo=month; NSCLC=non-small cell lung cancer; NSQ=non-squamous; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# OS in patients with and without treated brain metastases with OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo at 3 years[18,24]

## OS in patients with brain metastases: Extended follow-up analysis at 3 years[18,24*†]

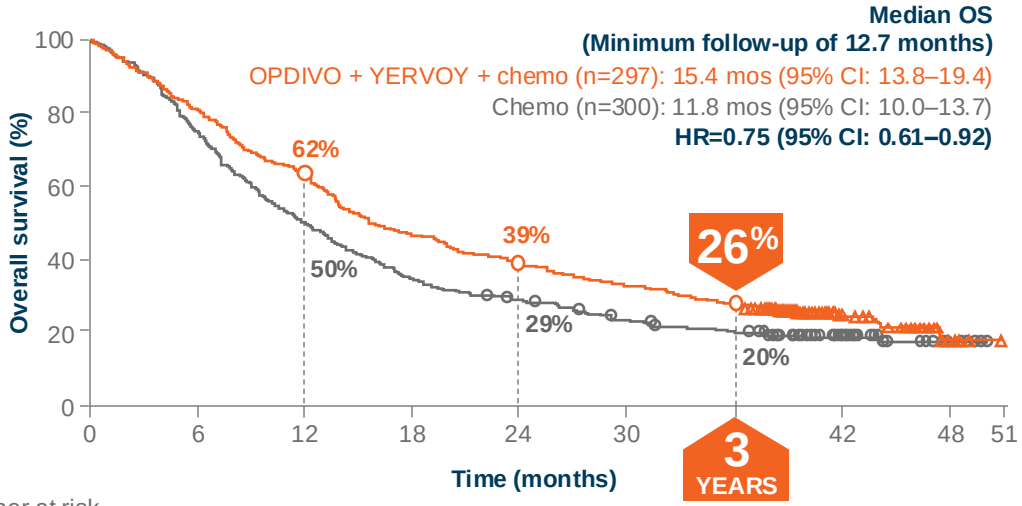



Number at risk

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 51 | 42 | 34 | 27 | 18 | 16 | 14 | 4 | 1 | 0 |
| Chemo | 50 | 28 | 13 | 8 | 6 | 6 | 6 | 2 | 1 | 0 |

- At the 36.1-month minimum follow-up, median OS for patients with brain metastases was 19.3 months (95% CI: 12.3–23.9) with OPDIVO + YERVOY with chemo and 6.8 months (95% CI: 4.7–9.7) with chemo; HR=0.45 (95% CI: 0.29–0.70)[24]

## OS in patients without brain metastases: Extended follow-up analysis at 3 years[18,24*‡]




Number at risk

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + YERVOY + chemo | 310 | 250 | 193 | 143 | 120 | 99 | 82 | 23 | 3 | 0 |
| Chemo | 308 | 232 | 155 | 107 | 87 | 68 | 57 | 26 | 4 | 0 |

- At the 36.1-month minimum follow-up, median OS for patients without brain metastases was 15.6 months (95% CI: 13.8–19.4) with OPDIVO + YERVOY with chemo and 12.1 months (95% CI: 10.2–13.7) with chemo; HR=0.80 (95% CI: 0.67–0.96)[24]

Minimum/median follow-up for OS: 36.1/42.6 months.[24]

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

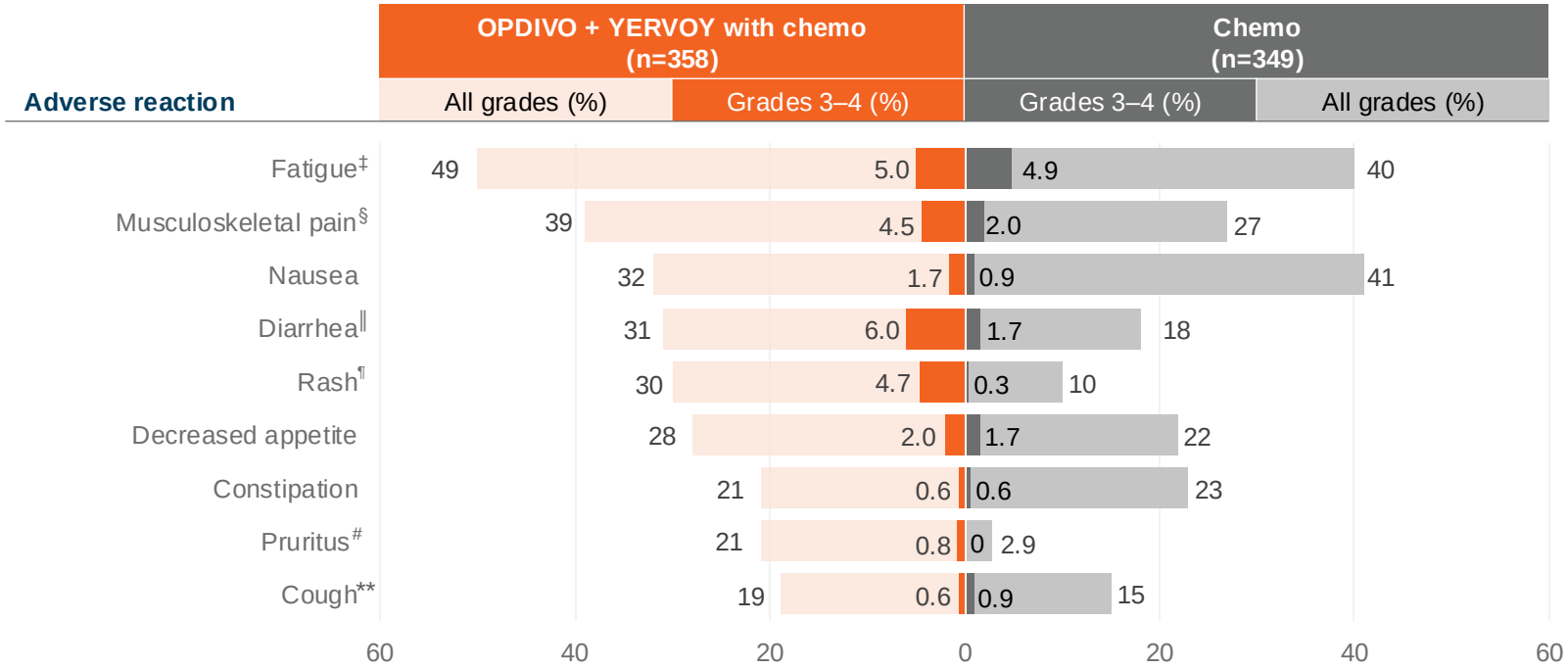
**OS: with and without brain metastases in PD-L1 <1%**

*Post hoc exploratory analysis.[24] †Subjects were eligible for enrollment in Checkmate 9LA if brain metastases were adequately treated and asymptomatic for at least 2 weeks prior to first treatment dose. In addition, subjects must have been either off corticosteroids, or on a stable or decreasing dose of ≤10 mg daily prednisone (or equivalent) for at least 2 weeks before first treatment. Subsequent radiotherapy was received by 20% (OPDIVO + YERVOY + chemo) and 24% (chemo); subsequent systemic therapy by 29% and 34%; subsequent immunotherapy by 4% and 26%; subsequent chemo by 29% and 16%, respectively.[24,25] ‡Subsequent radiotherapy was received by 17% (OPDIVO + YERVOY + chemo) and 16% (chemo); subsequent systemic therapy by 38% and 51%; subsequent immunotherapy by 9% and 38%; subsequent chemo by 35% and 29%, respectively.[24,,25]

CI=confidence interval; HR=hazard ratio; mo=month; NR=not reached; NSCLC=non-small cell lung cancer; OS=overall survival; PD-L1=programmed death ligand 1; r/m=recurrent or metastatic.

# The safety profile of OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo was consistent with the known profiles of each component[1,18*†]

## Adverse reactions in >10% of patients receiving OPDIVO + YERVOY and 2 cycles of chemo[1*]




Median number of doses was 9 for OPDIVO, 4 for YERVOY, and 2 cycles of chemo.[19]

### *Additional safety information*[1]

- OPDIVO + YERVOY with chemo was discontinued in 24% of patients due to adverse reactions and 56% had at least one dose withheld for an adverse reaction
- Serious adverse reactions occurred in 57% of patients who received OPDIVO + YERVOY with chemo
- 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

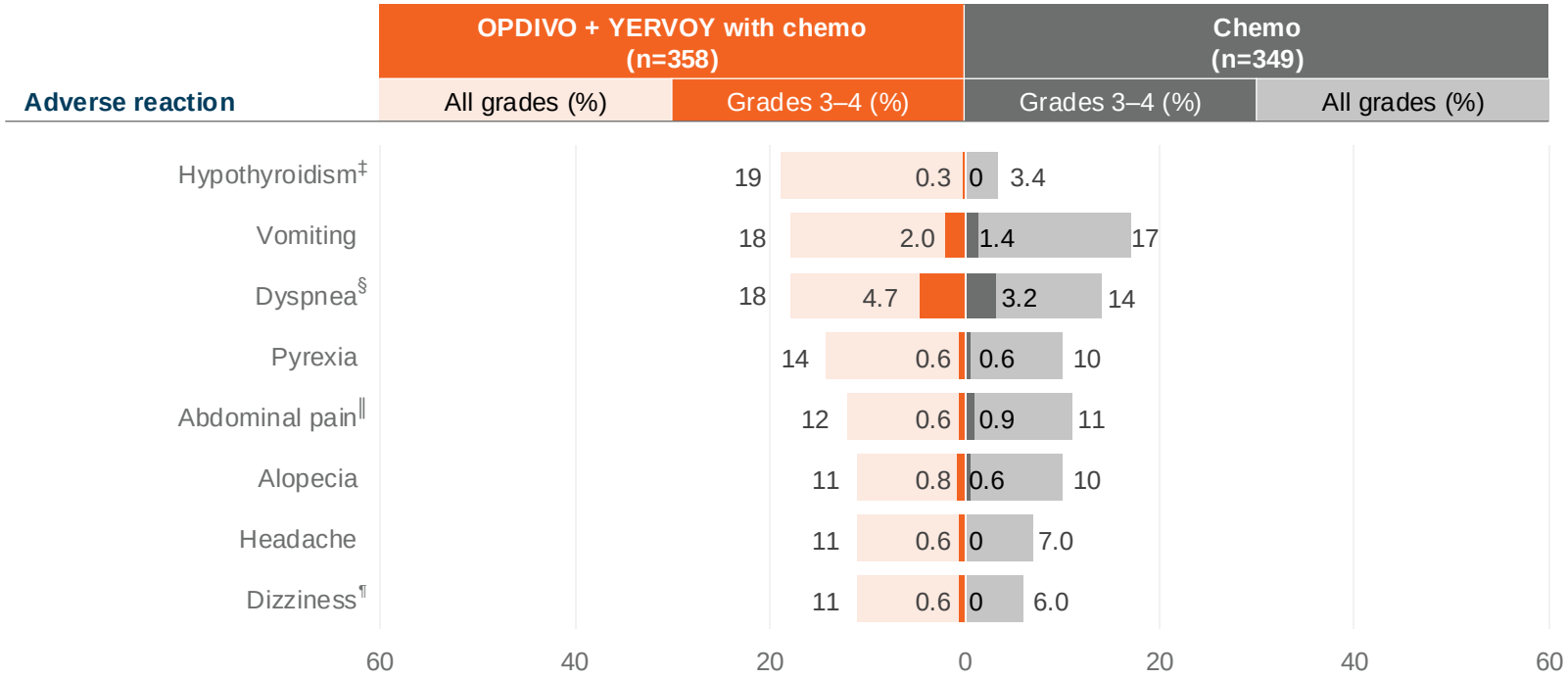
Toxicity was graded per NCI CTCAE v4.[1]

*In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in the comparator arm only); SQ: paclitaxel + carboplatin.[1] †Based on types of adverse reactions reported in 1L mNSCLC. Please note clinical trials are conducted under varying conditions, including different trial designs and dosing. Adverse reaction rates cannot be directly compared between trials.[1] ‡Includes fatigue and asthenia.[1] §Includes myalgia, back pain, pain in extremity, musculoskeletal pain, bone pain, flank pain, muscle spasms, musculoskeletal chest pain, musculoskeletal disorder, osteitis, musculoskeletal stiffness, non-cardiac chest pain, arthralgia, arthritis, arthropathy, joint effusion, psoriatic arthropathy, and synovitis.[1] ‖Includes colitis, ulcerative colitis, diarrhea, and enterocolitis.[1] ¶Includes acne, dermatitis, acneiform dermatitis, allergic dermatitis, atopic dermatitis, bullous dermatitis, generalized exfoliative dermatitis, eczema,keratoderma blennorrhagica, palmar-plantar erythrodysesthesia syndrome, rash, erythematous rash, generalized rash, macular rash, maculo-papular rash, morbilliform rash, papular rash, pruritic rash, skin exfoliation, skin reaction, skin toxicity, Stevens-Johnson syndrome, and urticaria.[1] #Includes pruritus and generalized pruritus.[1] **Includes cough, productive cough, and upper-airway cough syndrome.[1]

1L=first line; mNSCLC=metastatic NSCLC; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC=non-small cell lung cancer; NSQ=non-squamous; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

# The safety profile of OPDIVO® (nivolumab) + YERVOY® (ipilimumab) and 2 cycles of chemo was consistent with the known profiles of each component[1,18*†]

## Adverse reactions in >10% of patients receiving OPDIVO + YERVOY and 2 cycles of chemo (cont'd)[1*]




### *Additional safety information (cont'd)*

- The most common (>20%) adverse reactions were fatigue, musculoskeletal pain, nausea, diarrhea, rash, decreased appetite, constipation, and pruritus[1]
- At the minimum follow-up of 57.3 months, no new safety signals were identified[20]

With a minimum follow-up of 49.1 months, no new safety signals were identified for OPDIVO + YERVOY and 2 cycles of chemo.[23*]

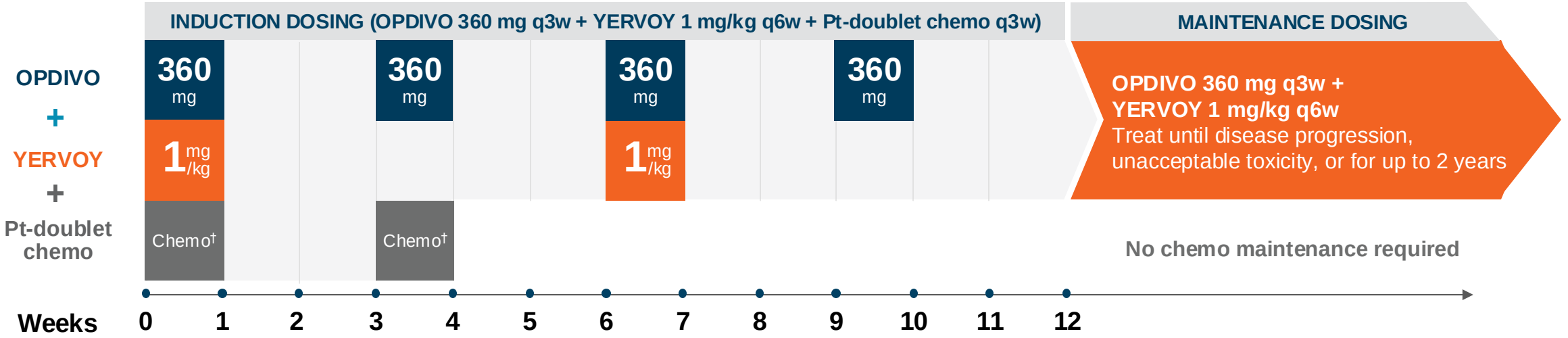
Toxicity was graded per NCI CTCAE v4.[1]

*In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in the comparator arm only); SQ: paclitaxel + carboplatin.[1] †Based on types of adverse reactions reported in 1L mNSCLC. Please note clinical trials are conducted under varying conditions, including different trial designs and dosing. Adverse reaction rates cannot be directly compared between trials.[1] ‡Includes autoimmune thyroiditis, increased blood thyroid stimulating hormone, hypothyroidism, thyroiditis, and decreased free tri-iodothyronine.[1] §Includes dyspnea, dyspnea at rest, and exertional dyspnea.[1] ‖Includes abdominal discomfort, abdominal pain, lower abdominal pain, upper abdominal pain, and gastrointestinal pain.[1] ¶Includes dizziness, vertigo, and positional vertigo.[1]

1L=first line; mNSCLC=metastatic NSCLC; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC=non-small cell lung cancer; NSQ=non-squamous; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

CM 9LA IMAR Summary

# Dosing: OPDIVO® (nivolumab) + low-dose (1 mg/kg) YERVOY® (ipilimumab) and 2 cycles of chemo[1,5*†]




- OPDIVO is administered as an IV infusion over 30 minutes[1]
- YERVOY is administered as an IV infusion over 30 minutes[5]

*For the r/m NSCLC dosing regimen in combination with chemo: 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.[1] †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.[1]

AUC=area under the curve; IV=intravenous; NSCLC=non-small cell lung cancer; NSQ=non-squamous; PD-L1=programmed death ligand 1; Pt=platinum; q3w=every 3 weeks; q6w=every 6 weeks; r/m=recurrent or metastatic; SQ=squamous.

# National Comprehensive Cancer Network® (NCCN®) recommendations for patients with metastatic NSCLC, regardless of PD-L1 expression[1,26]

**NCCN Category 1**

**Nivolumab (OPDIVO) + ipilimumab (YERVOY) + platinum-doublet chemotherapy*** is recommended as a Category 1, other recommended, first-line therapy option for eligible patients with metastatic NSCLC **regardless of PD-L1 expression and with performance status 0–1 (PD-L1 <1%) or 0–2 (PD-L1 ≥1%)** (V10.2024), who are *EGFR, ALK, ROS1, BRAF V600E, NTRK1/2/3, METex14,* and *RET* negative, and with no contraindications to PD-1 or PD-L1 inhibitors.[26]

Please see updated NCCN Guidelines® for a complete listing of all NCCN-recommended agents, including preferred options.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibilityfor their application or use in any way.

*Histology-based chemotherapy; NSQ: pemetrexed + (carboplatin or cisplatin); SQ: paclitaxel + carboplatin.[1]

ALK=anaplastic lymphoma kinase; BRAF=v-raf murine sarcoma viral oncogene homolog B; EGFR=epidermal growth factor receptor; mNSCLC=metastatic non-small cell lung cancer; NCCN=National Comprehensive Cancer Network; NSCLC=non-small cell lung cancer; NSQ=non-squamous; NTRK=neurotrophic tyrosine receptor kinase; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; ROS1=ROS proto oncogene 1, receptor tyrosine kinase; SQ=squamous.

# Their PD-L1 <1% deserves your 100%

OPDIVO (nivolumab) + YERVOY (ipilimumab) and 2 CYCLES OF CHEMO*

## Durable OS and response in patients with PD-L1 <1% at 5 years[20]*

- **22%** (n=22) of patients with **PD-L1 <1%** were alive at **5 years** and 8% (n=8) with chemo[20]
- **25%** of patients with **PD-L1 <1%** were still in response at **5 years** and 0% with chemo[20]

**OPDIVO® + YERVOY® and 2 cycles of chemo[1,21]*:**

- **Primary analysis** from the pre-specified interim 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 and 10.7 months (95% CI: 9.5–12.5) with chemo; HR=0.69 (96.71% CI: 0.55–0.87); *P*=0.0006
- Efficacy results from the pre-specified interim analysis when 351 events were observed (87% of the planned number of events for final analysis) with an 8.1-month minimum follow-up
- **Extended follow-up analysis**: with a minimum 57.3-month follow-up, median OS was 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=0.73 (95% CI: 0.62–0.85)[20]
  - At the 57.3-month minimum follow-up, median OS for PD-L1 <1% was 17.7 months (95% CI: 13.7–20.3) with OPDIVO + YERVOY with chemo and 9.8 months (95% CI: 7.7–13.5) with chemo; HR=0.63 (95% CI: 0.49–0.83)
  - At the 57.3-month minimum follow-up, median OS for PD-L1 ≥1% was 15.8 months (95% CI: 13.8–22.2) with OPDIVO + YERVOY with chemo and 10.9 months (95% CI: 9.5–13.2) with chemo; HR=0.73 (95% CI: 0.59–0.90)

**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.

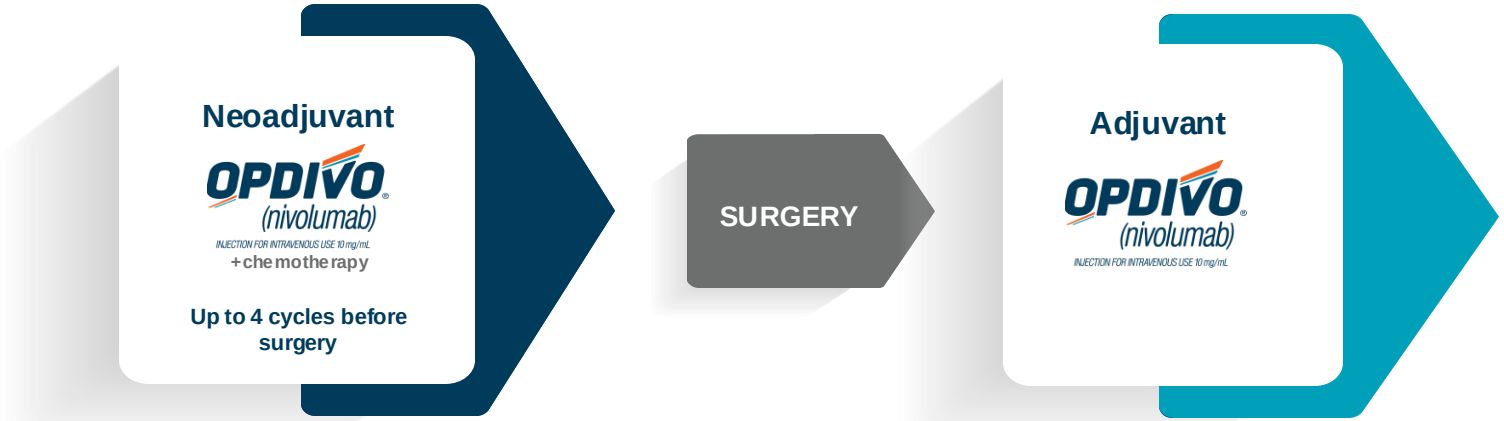
*vs chemo. In Checkmate 9LA, patients received 2 cycles of platinum-doublet chemo q3w in the experimental arm and 4 cycles in the comparator arm; NSQ: pemetrexed + carboplatin or cisplatin (optional pemetrexed maintenance therapy in comparator arm only); SQ: paclitaxel + carboplatin[1]

CI=confidence interval; HR=hazard ratio; NSCLC=non-small cell lung cancer; NSQ=non-squamous; OS=overall survival; PD-L1=programmed death ligand 1; q3w=every 3 weeks; r/m=recurrent or metastatic; SQ=squamous.

Please see Important Safety Information for OPDIVO® (nivolumab) and YERVOY® (ipilimumab) at the end of the presentation and US Full Prescribing Information for OPDIVO and YERVOY provided at this presentation.

## *CHECKMATE 77T: NOW APPROVED FOR THE PERIOPERATIVE TREATMENT OF RESECTABLE NSCLC*

# SEE THE IMPACT OF pCR IN YOUR PATIENTS




## With OPDIVO®, 25% of patients achieved pCR[1,2]

**Limitation:** The pCR rate was assessed in a descriptive analysis of a pre-specified secondary endpoint; the statistical testing plan did not assign alpha control to this endpoint, so direct comparisons between the treatment arms cannot be made.[1,2]

- **Checkmate 77T primary endpoint**: Median EFS at the 15.7-month minimum follow-up (median 25.4 months) for patients receiving neoadjuvant OPDIVO + chemo with adjuvant OPDIVO was not reached (95% CI: 28.9–NR) and 18.4 months (95% CI: 13.6–28.1) for those receiving neoadjuvant placebo + chemo with adjuvant placebo[1,2]
- **Checkmate 77T prespecified secondary endpoint**: pCR at the 15.7-month minimum follow-up (median 25.4 months) for patients receiving neoadjuvant OPDIVO + chemo with adjuvant OPDIVO was 25% (n=58/229; 95% CI: 20–31) and 4.7% (n=11/232; 95% CI: 2.4–8) for those receiving neoadjuvant placebo + chemo with adjuvant placebo[1,2]

### Your choice for chemo flexibility: OPDIVO was studied using both carboplatin- and cisplatin-based doublet therapy[1]

**Indication:** OPDIVO®, in combination with platinum-doublet chemotherapy, is indicated for neoadjuvant treatment of adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, followed by single-agent OPDIVO® as adjuvant treatment after surgery.

*NSQ: cisplatin + pemetrexed, carboplatin + pemetrexed, or carboplatin + paclitaxel; SQ: cisplatin + docetaxel or carboplatin+ paclitaxel.[3]
ALK=anaplastic lymphoma kinase; CI=confidence interval; EFS=event-free survival; EGFR=epidermal growth factor receptor; NR=not reached; NSCLC=non-small cell lung cancer; NSQ=non-squamous; pCR=pathological complete response; SQ=squamous.

Please see Important Safety Information for OPDIVO® (nivolumab) at the end of the presentation and US Full Prescribing Information for OPDIVO provided at this presentation.

# Patient case*

Alex
Age: 64

## Meet Alex, newly diagnosed with NSCLC, expressing PD-L1 1–49%

Alex is a 64-year-old retired certified public accountant who quit smoking 15 years ago. They have hypertension and generalized anxiety disorder.

They visited their doctor recently with some concerning symptoms, such as shortness of breath, chest pain, cough, and fatigue.

**What would you recommend as an appropriate treatment option for Alex?**

## Key patient information

### Biomarkers

- **PD-L1 expression: 1–49%**
- Negative for *EGFR, ALK, BRAF, KRAS, METex14, RET, ERBB2 (HER2), ROS1* rearrangement, and *NTRK1/2/3* fusion

### Performance status

- ECOG PS: 0

### Imaging (PET/CT scan)

- Lesion in upper lobe of the right lung (4.8 cm)

### Lymph node involvement

- Ipsilateral, multiple mediastinal lymph nodes

Initial diagnosis ▶ Lymph node involvement | Stage IIIB (T3N2) NSCLC

*Hypothetical patient case.

ALK=anaplastic lymphoma kinase; CT=computed tomography; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; ERBB2=v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2; HER2=human epidermal growth factor receptor 2; KRAS=Kirsten rat sarcoma; METex14=MET exon 14; NSCLC=non-small cell lung cancer; NTRK=neurotrophic tyrosine receptor kinase; PD-L1=programmed death ligand 1; PET=positron emission tomography; RET=rearranged during transfection proto oncogene, receptor tyrosine kinase; ROS1=ROS proto oncogene 1, receptor tyrosine kinase.

# Discussion questions

- What treatment options would your multidisciplinary team consider for Alex?
- What factors would you take into account for the final decision?

NSCLC=non-small cell lung cancer.

# Recent research* has shown that pCR could be an early indicator for long-term survival outcomes[4-8]


In a 2023 meta-analysis of 66 studies evaluating outcomes in the neoadjuvant treatment of patients with resectable NSCLC**, a positive correlation was seen between pCR and long-term survival outcomes**.[5]

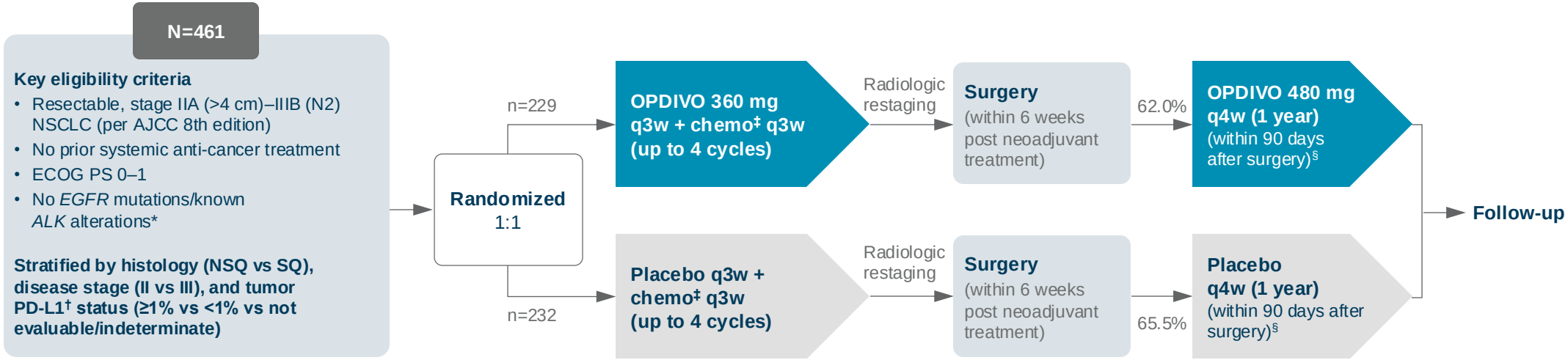
- pCR was associated with higher EFS (HR=0.25; 95% CI: 0.15–0.43)

***Limitation:** These post hoc exploratory meta-analyses do not substitute for randomized clinical trial evidence and cannot be used to draw definitive conclusions.

**Study design:** For this meta-analysis, a systematic literature review was conducted in the MEDLINE, CENTRAL, and EMBASE databases, as well as the proceedings from key annual meetings. The PRISMA and MOOSE guidelines for meta-analyses were followed. A total of 66 studies were included (8 randomized trials, 39 prospective nonrandomized trials, and 19 retrospective studies). Studies were included based on the following criteria: stage I–III NSCLC with intent to perform resection; delivery of PD-1, PD-L1, or CTLA-4 inhibitors before resection; and sufficient data for quantitative meta-analysis for at least one outcome measure (eg, DFS, PFS, EFS, RFS, or OS). For the purposes of this meta-analysis, PFS, DFS, EFS, and RFS were used interchangeably. This meta-analysis aimed to assess the safety and efficacy of I-O ± chemotherapy in the neoadjuvant setting, compare the safety and efficacy of neoadjuvant I-O + chemo vs chemo alone, and explore predictors of pCR with neoadjuvant I-O and their association with outcomes (PFS and OS). As this was not an individual patient data meta-analysis, no central review of pathology or radiology could be done.[5]

CI=confidence interval; CTLA-4=cytotoxic T-lymphocyte antigen 4; DFS=disease-free survival; EFS=event-free survival; HR=hazard ratio; I-O=immuno-oncology; MOOSE=Meta-Analysis of Observational Studies in Epidemiology; NSCLC=non-small cell lung cancer; OS=overall survival; pCR=pathologic complete response; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; PFS=progression-free survival; PRISMA=Preferred Reporting Items for Systematic reviews and Meta-Analyses; RFS=recurrence-free survival.

# Perioperative OPDIVO® (nivolumab): Studied in patients with stage IIA–IIIB NSCLC[1-3]




## OPDIVO was studied using both carboplatin- and cisplatin-based doublet therapy[1]

- **Primary endpoint:**
  - **EFS (by BICR):** Time from randomization to disease progression that precludes surgery, disease progression/recurrence after surgery, progression for patients without surgery, or death due to any cause[1,2,9]
- **Select prespecified secondary endpoint:**
  - **pCR‖ (by BIPR):** 0% residual viable tumor cells in both the primary tumor (lung) and sampled lymph nodes[1,2,9]
- The median number of adjuvant doses received was 13 (range: 1–13) in both OPDIVO + chemo/OPDIVO and placebo + chemo/placebo arms[3]

*_EGFR_ testing was mandatory in all patients with NSQ histology. _ALK_ testing was done in patients with a history of _ALK_ alterations. _EGFR_/_ALK_ testing was performed using US FDA/local health authority–approved assays.[3] †Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako).[3] ‡NSQ: cisplatin + pemetrexed, carboplatin + pemetrexed, or carboplatin + paclitaxel; SQ: cisplatin + docetaxel or carboplatin + paclitaxel.[3] §Until disease progression, recurrence, or unacceptable toxicity or for up to 1 year (13 cycles) post surgery.[1] ‖Assessed per immune-related pathologic response criteria.[3]
AJCC=American Joint Committee on Cancer; ALK=anaplastic lymphoma kinase; BICR=blinded independent central review; BIPR=blinded independent pathological review; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EFS=event-free survival; EGFR=epidermal growth factor receptor; IHC=immunohistochemistry; NSCLC=non-small cell lung cancer; NSQ=non-squamous; pCR=pathologic complete response; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; q3w=every 3 weeks; q4w=every 4 weeks; SQ=squamous.

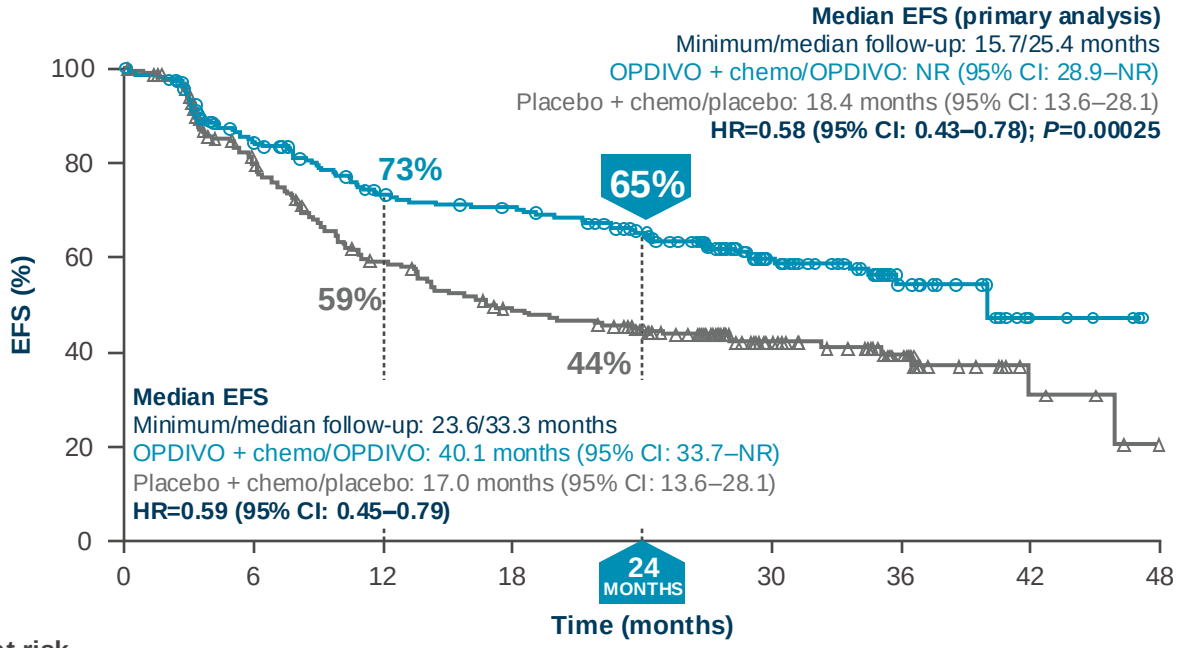
# Checkmate 77T baseline characteristics[10]

| Characteristics | OPDIVO® (nivolumab) + chemo/OPDIVO (n=229) | Placebo + chemo/placebo (n=232)* |
|---|---|---|
| **Median age, years (range)** | 66 (37–83) | 66 (35–86) |
| **Male, %** | 73 | 69 |
| **ECOG PS, %** | | |
| 0 | 64 | 61 |
| 1 | 36 | 39 |
| **Disease stage,† %** | | |
| IIA–B‡ | 35 | 35 |
| IIIA–B§ | 64 | 64 |
| **Histology, %** | | |
| Squamous | 51 | 51 |
| Non-squamous | 49 | 49 |
| **Smoking status, %** | | |
| Current/former | 93 | 88 |
| Never | 7 | 12 |
| **Tumor PD-L1 expression,‖ %** | | |
| Not evaluable | 4 | 5 |
| <1% | 41 | 40 |
| ≥1% | 56 | 55 |
| 1–49% | 36 | 33 |
| ≥50% | 20 | 22 |
| **Platinum therapy type, %** | | |
| Cisplatin | 24 | 18 |
| Carboplatin | 73 | 78 |
| **Geographic region, %** | | |
| North America | 10 | 9 |
| Europe | 54 | 55 |
| Asia | 28 | 22 |
| Rest of the world¶ | 8 | 15 |

Percentages may not total 100 due to rounding. *One patient had *EGFR* mutation and *ALK* translocation.[10] †Disease stage (per AJCC 8th edition) as reported in case report forms. Two (1%) patients in the OPDIVO + chemo/OPDIVO arm had stage IIIC disease, and 2 (1%) patients in the placebo + chemo/placebo arm had stage IV disease.[10] ‡Stage IIA was reported in 7% of patients in the OPDIVO + chemo/OPDIVO arm and 8% of patients in the placebo + chemo/placebo arm; stage IIB disease was reported in 29% and 27% of patients, respectively.[10] §Stage IIIA was reported in 45% of patients in the OPDIVO + chemo/OPDIVO arm and 49% of patients in the placebo + chemo/placebo arm; stage IIIB disease was reported in 19% and 15% of patients, respectively.[10] ‖Determined using the PD-L1 IHC 28-8 pharmDx assay (Dako).[10] ¶Includes only Argentina, Australia, Brazil, and Mexico.[10]
AJCC=American Joint Committee on Cancer; ALK=anaplastic lymphoma kinase; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; IHC=immunohistochemistry; PD-L1=programmed death ligand 1.

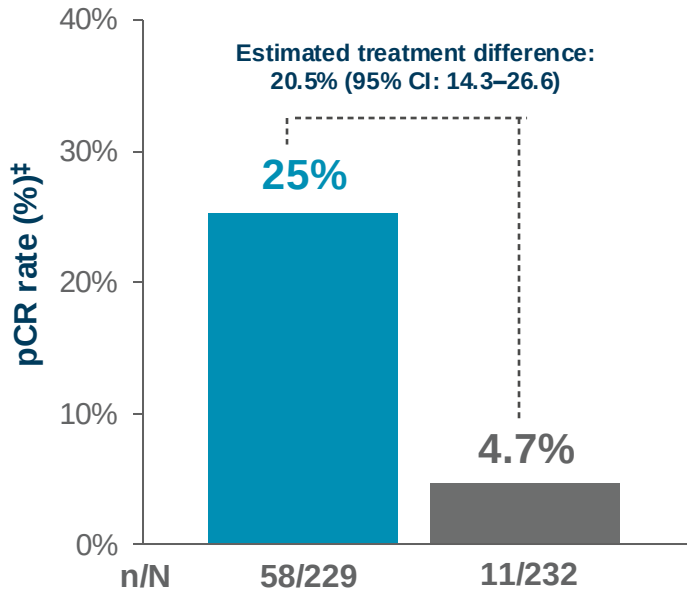
# Give patients the opportunity for an extended EFS benefit*† and a high pCR‡ rate with perioperative OPDIVO® (nivolumab)[1,2]

## EFS per BICR[1,2,11§]




| No. at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| OPDIVO + chemo/ OPDIVO | 229 | 172 | 140 | 132 | 114 | 63 | 26 | 5 | 0 |
| Placebo + chemo/ placebo | 232 | 164 | 117 | 92 | 78 | 39 | 22 | 5 | 0 |

## pCR per BIPR[1,2§]




**Only OPDIVO** gives **1** in **4** patients a chance at pCR

■OPDIVO + chemo/OPDIVO (95% CI: 20–31)

■Placebo + chemo/placebo (95% CI: 2.4–8)

Minimum/median follow-up: 15.7/25.4 months.[2]

**Limitation:** The pCR rate was assessed in a descriptive analysis of a pre-specified secondary endpoint; the statistical testing plan did not assign alpha control to this endpoint, so direct comparisons between the treatment arms cannot be made.

*vs chemo with placebo.[1,2] †EFS per BICR is defined as time from randomization to disease progression that precludes surgery, disease progression/recurrence after surgery, progression for patients without surgery, or death due to any cause.[1,2,9] ‡pCR by BIPR is defined as 0% residual viable tumor cells in both the primary tumor (lung) and sampled lymph nodes.[2,9] §Per the 8th edition American Joint Committee on Cancer.[1,2]
BICR=blinded independent central review; BIPR=blinded independent pathological review; CI=confidence interval; EFS=event-free survival; HR=hazard ratio; NR=not reached; NSCLC=non-small cell lung cancer; pCR=pathologic complete response.

Please see Important Safety Information for OPDIVO® (nivolumab) at the end of the presentation and US Full Prescribing Information for OPDIVO provided at this presentation.

Efficacy by N2 status

EFS by pCR

# Perioperative OPDIVO® (nivolumab) has a well-known safety profile[1]*

## Most serious ARs[1]

### Neoadjuvant

- In Checkmate 77T, of the patients who received OPDIVO in combination with platinum-doublet chemotherapy as neoadjuvant treatment (n=228), 21% of patients experienced serious adverse reactions
- The most frequent (≥2%) serious adverse reaction was pneumonia. Fatal adverse events occurred in 2.2% of patients due to cerebrovascular accident, COVID-19 infection, hemoptysis, pneumonia, and pneumonitis (0.4% each)

### Adjuvant

- In the adjuvant phase of Checkmate 77T, of the patients who received OPDIVO (n=142), 22% of the patients experienced serious adverse reactions. The most frequent serious adverse reaction was pneumonitis/ILD (2.8%). One fatal adverse event due to COVID-19 occurred

## Most common ARs[12]

- In Checkmate 77T, the most common adverse reactions (reported in ≥20%) in patients receiving OPDIVO in combination with chemotherapy (n=228) were anemia (39.5%), constipation (32.0%), nausea (28.9%), fatigue (28.1%), alopecia (25.9%), and cough (21.9%)

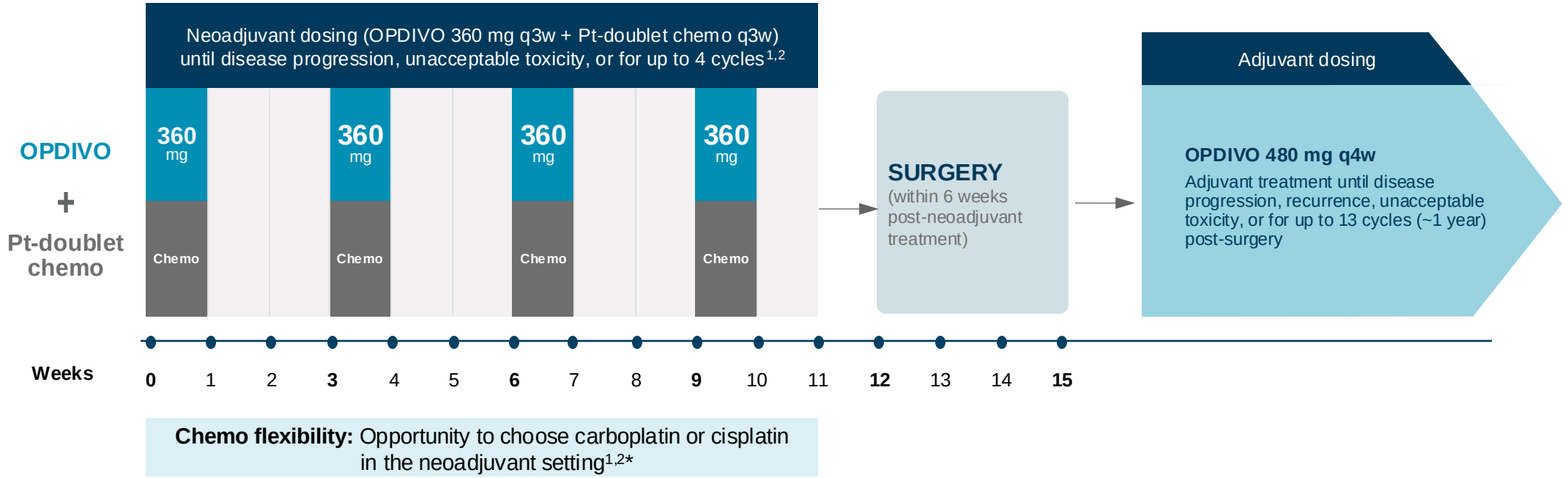
## Surgery-related ARs[1]

### Neoadjuvant

- In Checkmate 77T, 5.3% (n=12) of the OPDIVO-treated patients who received neoadjuvant treatment did not receive surgery due to adverse reactions. The adverse reactions that led to cancellation of surgery in OPDIVO-treated patients were cerebrovascular accident, pneumonia, and colitis/diarrhea (2 patients each) and acute coronary syndrome, myocarditis, hemoptysis, pneumonitis, COVID-19, and myositis (1 patient each)

*ARs were categorized according to the *Medical Dictionary for Regulatory Activities*, version 26.0, and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.[3]
AR=adverse reaction; ILD=interstitial lung disease.

# Dosing: Up to 4 cycles of OPDIVO® (nivolumab) + chemo prior to surgery and OPDIVO every 4 weeks post-surgery[1,2]

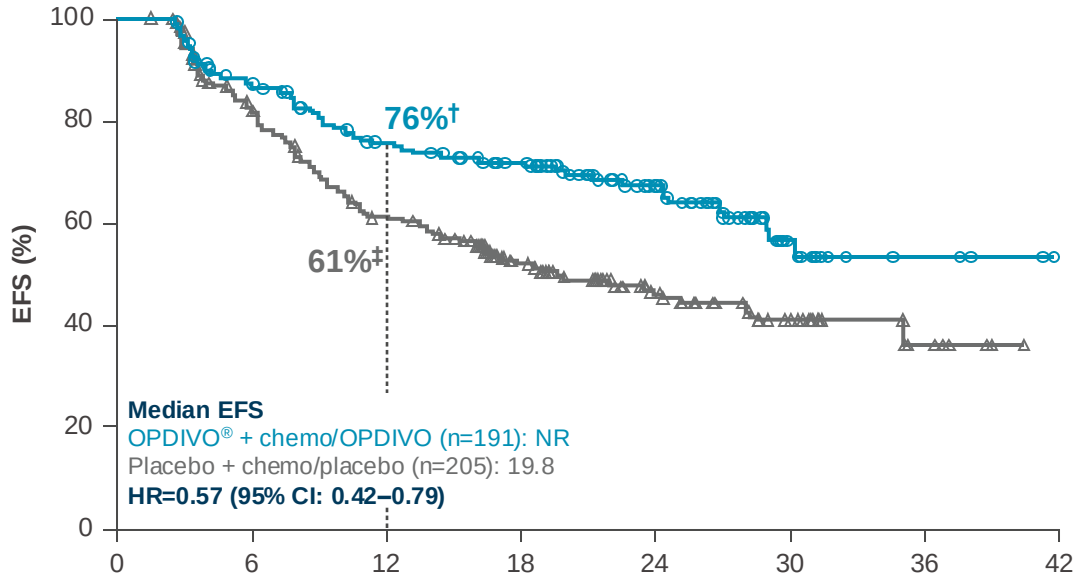



- OPDIVO is administered as an IV infusion over 30 minutes[1]
- Refer to the respective Prescribing Information for each therapeutic agent for the recommended dosage and administration information, as appropriate
- Administer OPDIVO first, followed by platinum-doublet chemo on the same day[1]
- No premedication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

*Any histology: paclitaxel and carboplatin; NSQ: pemetrexed and cisplatin or carboplatin; SQ: cisplatin and docetaxel.[1]
IV=intravenous; NSQ: non-squamous; Pt=platinum; q3w=every 3 weeks; q4w=every 4 weeks; SQ: squamous.
Please see Important Safety Information for OPDIVO® (nivolumab) at the end of the presentation and US Full Prescribing Information for OPDIVO provided at this presentation.

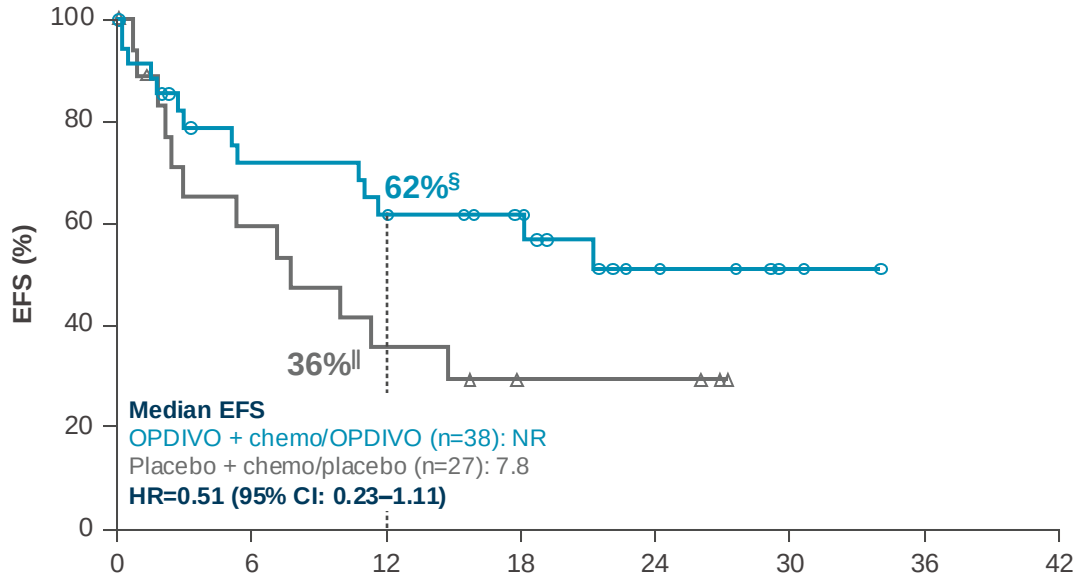
# EFS* by number of completed neoadjuvant treatment cycles[13]

## 4 cycles




| No. at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OPDIVO + chemo/ OPDIVO | 191 | 152 | 123 | 101 | 63 | 18 | 4 | 0 |
| Placebo + chemo/ placebo | 205 | 155 | 112 | 75 | 41 | 19 | 6 | 0 |

## < 4 cycles




| No. at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OPDIVO + chemo/ OPDIVO | 38 | 21 | 18 | 14 | 6 | 2 | 0 | 0 |
| Placebo + chemo/ placebo | 27 | 10 | 6 | 3 | 3 | 0 | 0 | 0 |

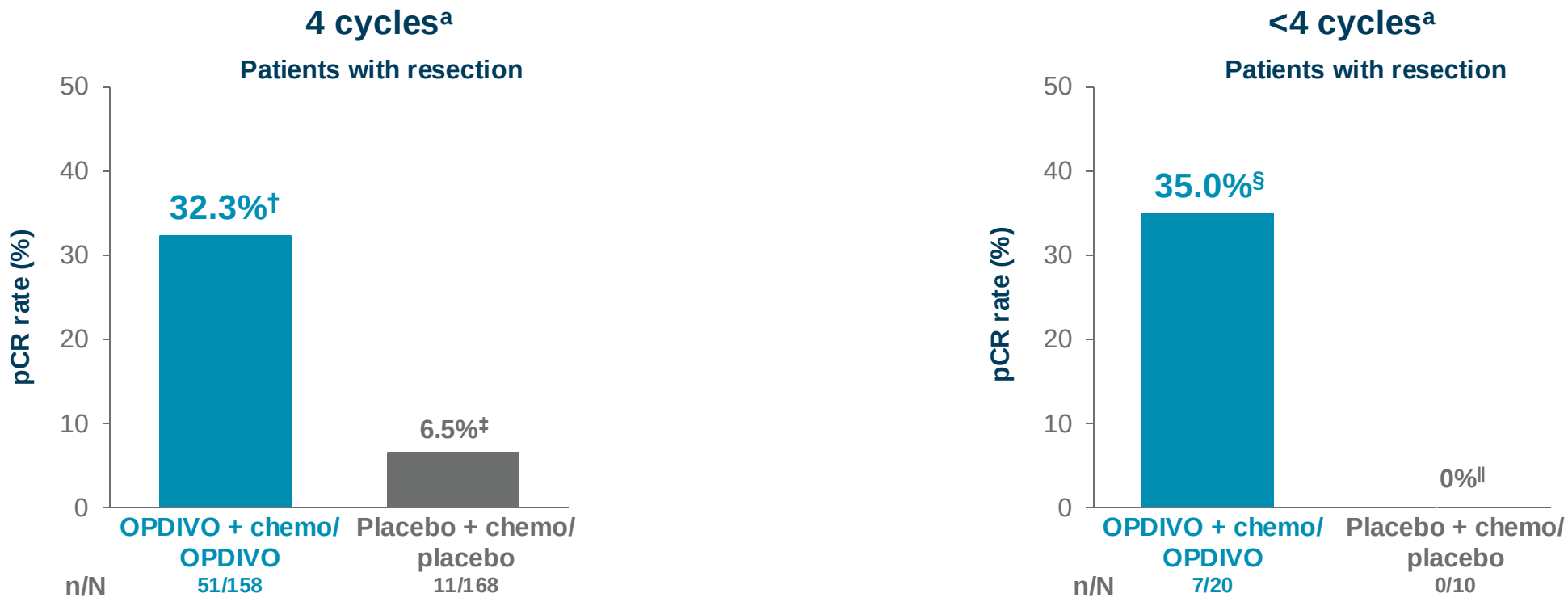
**Limitation:** Checkmate 77T was not powered to detect differences in EFS by number of completed neoadjuvant treatment cycle subgroups; therefore, this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroup.

Minimum/median follow-up: 15.7/25.4 months.[13]

*EFS per BICR is defined as time from randomization to disease progression that precludes surgery, disease progression/recurrence after surgery, progression for patients without surgery, or death due to any cause.[2] †95% CI: 68–81.[13] ‡95% CI: 54–68.[13] §95% CI: 42–76.[13] ‖95% CI: 15–57.[13]

BICR=blinded independent central review; CI=confidence interval; EFS=event-free survival; HR=hazard ratio; NR=not reached.

# pCR* by number of completed neoadjuvant treatment cycles[13]




**Limitation:** Checkmate 77T was not powered to detect differences in pCR by number of completed neoadjuvant treatment cycle subgroups; therefore, this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroup.

[a]Of the 7 patients with <4 neoadjuvant treatment cycles who had a pCR in the OPDIVO arm, 3 received 3 neoadjuvant cycles, and 4 received 2 neoadjuvant cycles.[13]

Minimum/median follow-up: 15.7/25.4 months.[13]

**pCR in ITT with 4 neoadjuvant cycles**

*pCR by BIPR is defined as 0% residual viable tumor cells in both the primary tumor (lung) and sampled lymph nodes.[2,9] †95% CI: 25.1–40.2.[13] ‡95% CI: 3.3–11.4.[13] §95% CI: 15.4–59.2.[13] ‖95% CI: 0–30.8.[13]
BIPR=blinded independent pathological review; CI=confidence interval; ITT=intent to treat; pCR=pathologic complete response.

# *Now* patients can start and stay the course with OPDIVO® (nivolumab) before and after surgery[1,2]

***NOW APPROVED:* CHECKMATE 77T**

**Neoadjuvant**

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

+chemotherapy

**Up to 4 cycles before surgery**

**SURGERY**

**Adjuvant**

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

**Superior EFS:**
**65% EFS with perioperative OPDIVO**
vs 44% with placebo + chemo
**at 24 months[11]***

**High pCR†:**
**25% pCR with perioperative OPDIVO**
and 4.7% with placebo + chemo[1,2‡]

**Options with OPDIVO[1]**

- **Studied using both carboplatin- and cisplatin-based doublet therapy**
- **Only I-O approved for neoadjuvant-only[§] and perioperative regimens**
- **Provides dosing data on up to 4 neoadjuvant cycles of treatment in the perioperative regimen[‖]**

**Checkmate 77T appendix**

**Checkmate 816**

- Median EFS at the 33.3-month median follow-up for patients receiving neoadjuvant OPDIVO + chemo with adjuvant OPDIVO was 40.1 months (95% CI: 33.7–NR) vs 17.0 months (95% CI: 13.6–28.1) for those receiving neoadjuvant placebo + chemo with adjuvant placebo[11]
- At the 25.4-month median follow-up, the hazard ratio was 0.14 (95% CI: 0.06–0.35) for patients with pCR vs those without pCR who received neoadjuvant OPDIVO + chemo with adjuvant OPDIVO and 0.32 (95% CI: 0.10–1.00) for patients with pCR vs those without pCR who received neoadjuvant placebo + chemo with adjuvant placebo[10]

**‡Limitation:** The pCR rate was assessed in a descriptive analysis of a pre-specified secondary endpoint; the statistical testing plan did not assign alpha control to this endpoint, so direct comparisons between the treatment arms cannot be made.
**‖Limitation:** Checkmate 77T was not powered to detect differences in EFS and pCR by number of completed neoadjuvant treatment cycle subgroups; therefore, this exploratory analysis should be interpreted with caution because of the limited patient numbers and potential imbalances in baseline characteristics within the subgroups.

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

*Minimum/median follow-up: 23.6/33.3 months.[11] †Minimum/median follow-up: 15.7/25.4 months.[13]
CI=confidence interval; EFS=event-free survival; NR=not reached; pCR=pathologic complete response.
Please see Important Safety Information for OPDIVO® (nivolumab) at the end of the presentation and US Full Prescribing Information for OPDIVO provided at this presentation.

# Important Safety Information

## Severe and Fatal Immune-Mediated Adverse Reactions

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

(continued on next slide)

# Important Safety Information (cont'd)

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

### 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%).

### 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%).

### 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.

(continued on next slide)

# Important Safety Information (cont'd)

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

### Immune-Mediated Endocrinopathies (cont'd)

- In patients receiving OPDIVO® monotherapy, adrenal insufficiency occurred in 1% (20/1994), including Grade 3 (0.4%) and Grade 2 (0.6%).
- In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients, including Grade 3 (0.2%) and Grade 2 (0.3%).
- In patients receiving OPDIVO monotherapy, thyroiditis occurred in 0.6% (12/1994) of patients, including Grade 2 (0.2%).
- In patients receiving OPDIVO monotherapy, hyperthyroidism occurred in 2.7% (54/1994) of patients, including Grade 3 (<0.1%) and Grade 2 (1.2%).
- In patients receiving OPDIVO monotherapy, hypothyroidism occurred in 8% (163/1994) of patients, including Grade 3 (0.2%) and Grade 2 (4.8%).
- In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients, including Grade 3 (0.4%) and Grade 2 (0.3%), and 2 cases of diabetic ketoacidosis.

### Immune-Mediated Nephritis with Renal Dysfunction

- OPDIVO 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%).

(continued on next slide)

# Important Safety Information (cont'd)

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

### 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%).

(continued on next slide)

# Important Safety Information (cont'd)

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

### Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received OPDIVO® monotherapy or 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, other transplant (including corneal graft) 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.

(continued on next slide)

# Important Safety Information (cont'd)

## 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.

## 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.

(continued on next slide)

# Important Safety Information (cont'd)

## 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.

(continued on next slide)

# Important Safety Information (cont'd)

## 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. In Checkmate 77T, serious adverse reactions occurred in 21% of patients who received OPDIVO in combination with platinum-doublet chemotherapy as neoadjuvant treatment (n=228). The most frequent (≥2%) serious adverse reaction was pneumonia. Fatal adverse reactions occurred in 2.2% of patients due to cerebrovascular accident, COVID-19 infection, hemoptysis, pneumonia, and pneumonitis (0.4% each). In the adjuvant phase of Checkmate 77T, 22% of patients experienced serious adverse reactions (n=142). The most frequent serious adverse reaction was pneumonitis/ILD (2.8%). One fatal adverse reaction due to COVID-19 occurred. 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.

(continued on next slide)

# Important Safety Information (cont'd)

## 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%). In Checkmate 77T, the most common adverse reactions (reported in ≥20%) in patients receiving OPDIVO in combination with chemotherapy (n=228) were anemia (39.5%), constipation (32.0%), nausea (28.9%), fatigue (28.1%), alopecia (25.9%), and cough (21.9%). 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%).

## Surgery Related Adverse Reactions

- In Checkmate 77T, 5.3% (n=12) of the OPDIVO-treated patients who received neoadjuvant treatment did not receive surgery due to adverse reactions. The adverse reactions that led to cancellation of surgery in OPDIVO-treated patients were cerebrovascular accident, pneumonia, and colitis/diarrhea (2 patients each) and acute coronary syndrome, myocarditis, hemoptysis, pneumonitis, COVID-19, and myositis (1 patient each).

## Clinical Trials and Patient Populations

- 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 816–neoadjuvant non-small cell lung cancer, in combination with platinum-doublet chemotherapy; Checkmate 77T–Neoadjuvant treatment with platinum-doublet chemotherapy for non-small cell lung cancer followed by single-agent OPDIVO as adjuvant treatment after surgery

# References: Checkmate 9LA


1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
2. Metro G, Ricciuti B, Brambilla M, et al. The safety of nivolumab for the treatment of advanced non-small cell lung cancer. *Expert Opin Drug Saf.* 2017;16(1):101-109.
3. Byrne EH, Fisher DE. Immune and molecular correlates in melanoma treated with immune checkpoint blockade. *Cancer*. 2017;123(S11):2143-2153.
4. Weber JS, Hamid O, Chasalow SD, et al. Ipilimumab increases activated T cells and enhances humoral immunity in patients with advanced melanoma. *J Immunother.* 2012;35(1):89-97.
5. YERVOY® (ipilimumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
6. Farber DL, Yudanin NA, Restifo NP. Human memory T cells: generation, compartmentalization and homeostasis. *Nat Rev Immunol.* 2014;14(1):24-35.
7. Ansell SM, Hurvitz SA, Koenig PA, et al. Phase I study of ipilimumab (MDX-010), an anti–CTLA-4 monoclonal antibody, in patients with relapsed and refractory B-cell non–Hodgkin lymphoma. *Clin Cancer Res.* 2009;15(20):6446-6453.
8. Felix J, Lambert J, Roelens M, et al. Ipilimumab reshapes T cell memory subsets in melanoma patients with clinical response. *Oncoimmunology*. 2016;5(7):1136045.
9. Pedicord VA, Montalvo W, Leiner IM, Allison JP. Single dose of anti–CTLA-4 enhances CD8+ T-cell memory formation, function, and maintenance. *Proc Natl Acad Sci U S A*. 2011;108(1):266-271.
10. Pico de Coaña YP, Wolodarski M, Poschke I, et al. Ipilimumab treatment decreases monocytic MDSCs and increases CD8 effector memory T cells in long-term survivors with advanced melanoma. *Oncotarget*. 2017;8(13):21539-21553.
11. Buchbinder EI, Desai A. CTLA-4 and PD-1 pathways: similarities, differences, and implications of their inhibition. *Am J Clin Oncol*. 2016;39(1):98-106.
12. Taube JM, Anders RA, Young GD, et al. Colocalization of inflammatory response with B7-H1 expression in human melanocytic lesions supports an adaptive resistance mechanism of immune escape. *Sci Transl Med*. 2012;4(127):127ra37.
13. Taube JM, Anders RA, Young GD, et al. Colocalization of inflammatory response with B7-H1 expression in human melanocytic lesions supports an adaptive resistance mechanism of immune escape. *Sci Transl Med*. 2012;4(127):127ra37 [supplementary appendix].
14. Liakou CI, Kamat A, Tang DN, et al. CTLA-4 blockade increases IFNγ-producing CD4+ICOShi in cells to shift the ratio of effector to regulatory T cells in cancer patients. *Proc Natl Acad Sci U S A*. 2008;105(39):14987-14992.
15. Data on file. BMS-REF-ONCO-0025. Princeton, NJ: Bristol-Myers Squibb Company; 2022.
16. Waterhouse D, Lam J, Betts KA, et al. Real-world outcomes of immunotherapy-based regimens in first-line advanced non-small cell lung cancer. *Lung Cancer*. 2021;156:41-49.
17. Skov BG, Rørvig SB, Jensen THL, et al. The prevalence of programmed death ligand-1 (PD-L1) expression in non-small cell lung cancer in an unselected, consecutive population. *Mod Pathol*. 2020;33(1):109-117.
18. Paz-Ares L, Ciuleanu TE, Cobo M, et al. First-line nivolumab plus ipilimumab combined with two cycles of chemotherapy in patients with non-small-cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial. *Lancet Oncol.* 2021;22(2):198-211.
19. Data on file. NIVO 562. Princeton, NJ: Bristol-Myers Squibb Company; 2020.
20. Reck M, Ciuleanu TE, Schenker M, et al. Five-year outcomes with first-line nivolumab plus ipilimumab with chemotherapy vs chemotherapy in patients with metastatic NSCLC in CheckMate 9LA. Poster presentation at ASCO 2024. Abstract 8560.

# References: Checkmate 9LA cont'd


21. Reck M, Ciuleanu TE, Cobo M, et al. First-line nivolumab plus ipilimumab with two cycles of chemotherapy versus chemotherapy alone (four cycles) in advanced non-small-cell lung cancer: CheckMate 9LA 2-year update. *ESMO Open*. 2021. doi:10.1016/j.esmoop.2021.100273.
22. Data on file. NIVO 566. Princeton, NJ: Bristol-Myers Squibb Company; 2020.
23. Carbone DP, Ciuleanu TE, Schenker M, et al. Four-year clinical update and treatment switching-adjusted outcomes with first-line nivolumab plus ipilimumab with chemotherapy for metastatic non-small cell lung cancer in the CheckMate 9LA randomized trial. *J Immunother Cancer.* 2024;12(2):e008189.
24. Paz-Ares LG, Ciuleanu TE, Cobo M, et al. First-line nivolumab plus ipilimumab with chemotherapy vs chemotherapy alone for metastatic non-small cell lung cancer in CheckMate 9LA: 3-year clinical update and outcomes in patients with brain metastases or select somatic mutations. *J Thorac Oncol*. 2023;18(2):204-222.
25. Paz-Ares LG, Ciuleanu TE, Cobo M, et al. First-line nivolumab plus ipilimumab with chemotherapy vs chemotherapy alone for metastatic non-small cell lung cancer in CheckMate 9LA: 3-year clinical update and outcomes in patients with brain metastases or select somatic mutations. *J Thorac Oncol*. 2023;18(2):204-222 [supplementary appendix].
26. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.10.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed Sept 23, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
27. John T, Ciuleanu TE, Cobo M, et al. Clinical outcomes in patients with tumor PD-L1 <1% with first-line nivolumab + ipilimumab + 2 cycles of chemotherapy vs chemotherapy alone for metastatic non-small cell lung cancer: results from CheckMate 9LA. Poster presented at ESMO 2022. Abstract 1049P.
28. Data on file. NIVO 561. Princeton, NJ: Bristol-Myers Squibb Company; 2020.

# References: Checkmate 77T


1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
2. Cascone T, Awad MM, Spicer JD, et al. Perioperative nivolumab in resectable lung cancer. *N Engl J Med*. 2024;390(19):1756-1769.
3. Cascone T, Awad MM, Spicer JD, et al. Perioperative nivolumab in resectable lung cancer. *N Engl J Med*. 2024;390(19):1756-1769 [supplementary appendix].
4. Nie R, Chen F, Provencio M, et al. Predictive value of radiological response, pathological response and relapse-free survival for overall survival in neoadjuvant immunotherapy trials: pooled analysis of 29 clinical trials. *Eur J Cancer*. 2023;186:211-221.
5. Wu Y, Verma V, Gay CM, et al. Neoadjuvant immunotherapy for advanced, resectable non-small cell lung cancer: a systematic review and meta-analysis. *Cancer*. 2023;129(13):1969-1985.
6. Saqi A, Leslie KO, Moreira AL, et al. Assessing pathological response in resected lung cancers: current standards, proposal for a novel pathological response calculator tool, and challenges in practice. *JTO Clin Res Rep*. 2022;3(5):1000310.
7. Travis WD, Dacic S, Wistuba I, et al. IASLC multidisciplinary recommendations for pathologic assessment of lung cancer resection specimens after neoadjuvant therapy. *J Thorac Oncol*. 2020;15(5):709–740.
8. Hines JB, Cameron RB, Esposito A, et al. Evaluation of major pathologic response and pathologic complete response as surrogate end points for survival in randomized controlled trials of neoadjuvant immune checkpoint blockade in resectable in NSCLC. *J Thorac Oncol.* 2024;19(7):1108-1116.
9. Cascone T, Awad MM, Spicer JD, et al. Perioperative nivolumab in resectable lung cancer. *N Engl J Med*. 2024;390(19):1756-1769 [protocol].
10. Cascone T, Awad MM, Spicer J, et al. CheckMate 77T: phase 3 study comparing neoadjuvant nivolumab plus chemotherapy vs neoadjuvant placebo plus chemotherapy followed by surgery and adjuvant nivolumab or placebo for previously untreated, resectable stage II–IIIB NSCLC. Oral presentation at ESMO 2023. Abstract LBA1.
11. Provencio Pulla M, Awad MM, Cascone T, et al. Perioperative nivolumab vs placebo in patients with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study. Oral presentation at ESMO 2024. Abstract LBA50.
12. Data on File. BMS-REF-NIVO-0293. Princeton, NJ: Bristol-Myers Squibb Company. 2024.
13. Awad MM, Cascone T, Spicer JD, et al. Clinical outcomes with perioperative nivolumab in patients with resectable NSCLC from the phase 3 CheckMate 77T study. Oral presentation at ELCC 2024. Abstract LBA2.
14. Provencio Pulla M, Awad MM, Spicer JD, et al. Clinical outcomes with perioperative nivolumab by nodal status among patients with stage III resectable NSCLC: results from the phase 3 CheckMate 77T study. Oral presentation at ASCO 2024. Abstract LBA8007.

# References: Checkmate 227


1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
2. YERVOY® (ipilimumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
3. Hellman MD, Paz-Ares L, Caro RB, et al. Nivolumab plus ipilimumab in advanced non–small-cell lung cancer. *N Engl J Med.* 2019;381(21):2020-2031.
4. Hellman MD, Paz-Ares L, Caro RB, et al. Nivolumab plus ipilimumab in advanced non–small-cell lung cancer. *N Engl J Med.* 2019;381(21):2020-2031 [supplementary appendix].
5. Ramalingam SS, Ciuleanu TE, Caro RB, et al. Six-year survival and health-related quality of life outcomes with first-line nivolumab plus ipilimumab in patients with metastatic NSCLC for CheckMate 227. Oral presentation at WCLC 2023. Abstract OA14.03.
6. American Cancer Society. Cancer facts & figures 2018. Cancer.org. 2018. Accessed May 24, 2022. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf.
7. Data on file. BMS-REF-ONCO-0244. Princeton, NJ: Bristol-Myers Squibb Company; 2022.
8. Brahmer JR, Lee JS, Ciuleanu TE, et al. Five-year survival outcomes with nivolumab plus ipilimumab versus chemotherapy as first-line treatment for metastatic non-small-cell lung cancer in CheckMate 227. *J Clin Oncol.* 2023;41(6):1200-1212 [supplementary appendix].
9. Provencio P, Ramalingam SS, Ciuleanu TE, et al. Nivolumab + ipilimumab versus platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: three-year update from CheckMate 227 Part 1. Poster presentation at GECP SLCG 2020.
10. Paz-Ares L, Ramalingam SS, Ciuleanu TE, et al. First-line nivolumab plus ipilimumab in advanced NSCLC: 4-year outcomes from the randomized, open label, phase 3 Checkmate 227 Part 1 trial. *J Thorac Oncol*. 2021;17(2):289-308.
11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.10.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed Sept 23, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
12. Data on file. NIVO 563. Princeton, NJ: Bristol-Myers Squibb Company; 2020.

# References: Checkmate 816


1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
2. Forde PM, Spicer J, Lu S, et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. *N Engl J Med*. 2022;386(21):1973-1985 [supplementary appendix].
3. Forde PM, Spicer J, Lu S, et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. *N Engl J Med*. 2022;386(21):1973-1985.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.10.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed Sept 23, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
5. 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.
6. Spicer JD, Girard N, Pulla MP, et al. Neoadjuvant nivolumab plus chemotherapy vs chemotherapy in patients with resectable NSCLC: 4-year update from CheckMate 816. Oral presentation at ASCO 2024. Abstract LBA8010.
7. Forde PM, Spicer J, Girard N, et al. Neoadjuvant nivolumab plus platinum-doublet chemotherapy for resectable NSCLC: 3-year update from CheckMate 816. Oral presentation at ELCC 2023. Abstract 84O.
8. Provencio-Pulla M, Forde PM, Spicer D, et al. Neoadjuvant nivolumab plus chemotherapy in the phase 3 CheckMate 816 study: 3-year results by tumor PD-L1 expression. Oral presentation at ESMO 2023. Abstract LBA57.
9. Spicer J, Wang C, Tanaka F, et al. Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer. Oral presentation at ASCO 2021. Abstract 8503.

# Thank you for attending today's program!
# Any questions?

For additional information,
please scan the QR code below:

# oncology exchange

fall 2024

## Clinical Session