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Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

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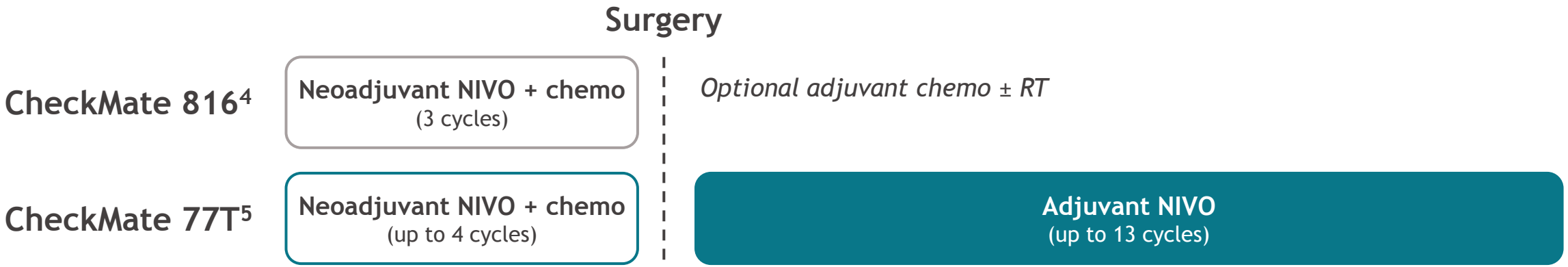
Introduction

- NIVO + chemo is an approved and guideline-recommended neoadjuvant-only immunotherapy-containing regimen for eligible patients with resectable NSCLC[1-3]
  - EFS benefit was demonstrated vs neoadjuvant chemo (HR = 0.63[a])[4]
- Perioperative NIVO built on neoadjuvant NIVO + chemo and demonstrated significant EFS benefit vs placebo (HR = 0.58[b])[5]
- pCR rates with neoadjuvant NIVO + chemo were 24%–25%[4,5]



[a]97.38% CI, 0.43-0.91. [b]97.36% CI, 0.42-0.81.

1. OPDIVO® (nivolumab) [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; February 2023. 2. OPDIVO® (nivolumab) [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb Pharma EEIG; July 2023. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer. V7.2024. ©National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 19, 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. 4. Forde PM, et al. *N Engl J Med* 2022;386:1973–1985. 5. Cascone T, et al. *N Engl J Med* 2024;390:1756–1769.

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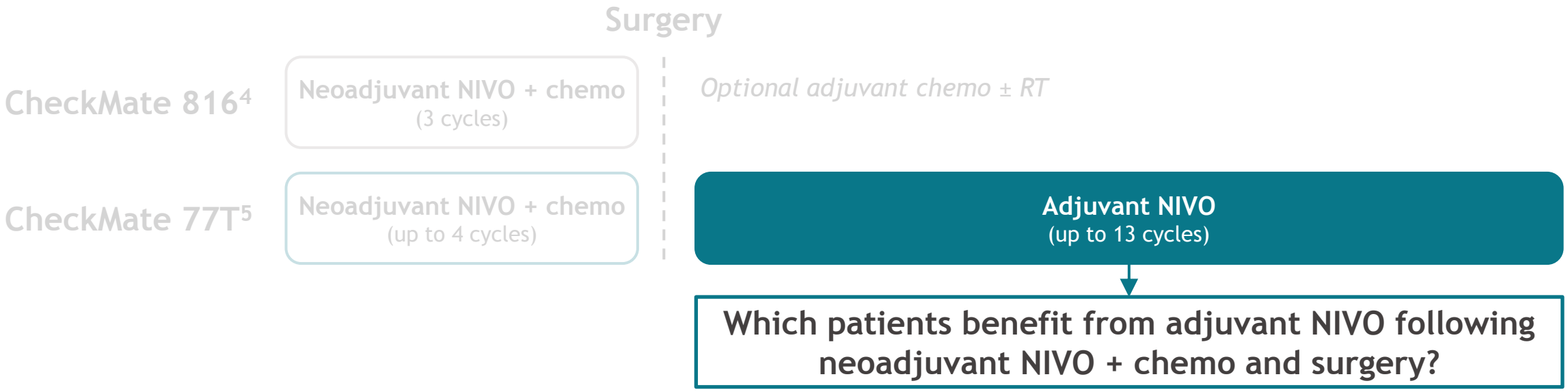

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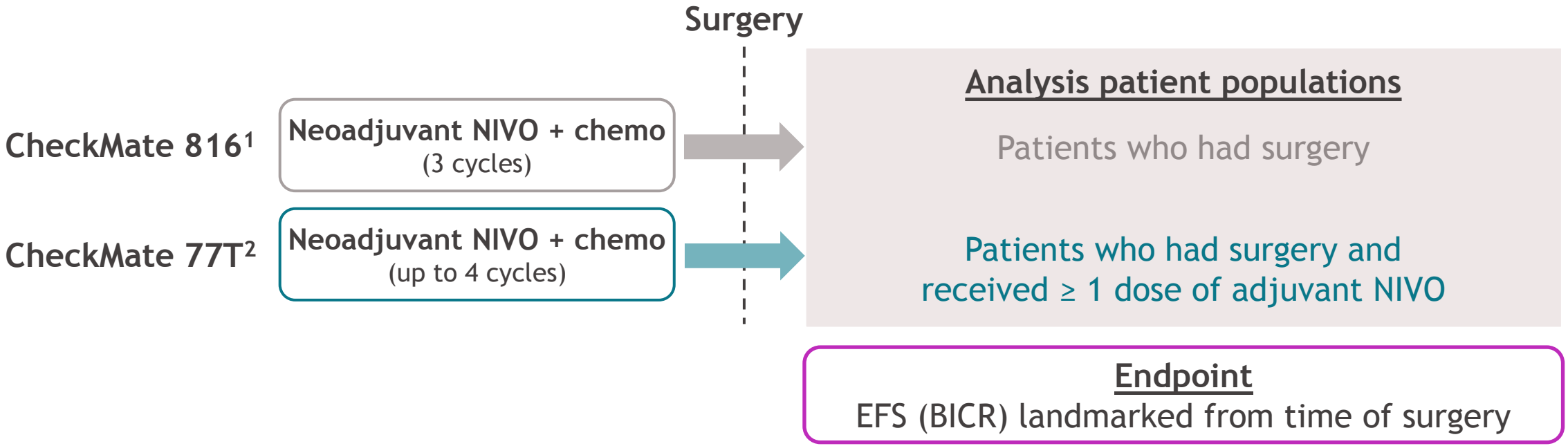
Methods: perioperative NIVO vs neoadjuvant NIVO + chemo



- In lieu of a head-to-head trial, exploratory propensity score weighting analyses (ATT[a] and ATE[b]) were performed to allow simplified reproduction of a randomized trial by adjusting for clinically relevant baseline demographics and disease characteristics[c] between study populations and reducing the confounding effects of these factors
  - Subgroup analyses were not weighted due to smaller sample sizes
- Median duration of follow-up[d]: 29.5 months (CheckMate 816) and 33.3 months (CheckMate 77T)

[a]Average treatment effect for the treated (ATT): a weight of 1 was applied to patients in the perioperative NIVO arm of CheckMate 77T; varying weights were applied to patients in the CheckMate 816 NIVO + chemo arm to make them comparable to those in the perioperative NIVO arm in CheckMate 77T based on propensity scores. [b]Average treatment effect (ATE): varying weights were applied to all patients in the populations of interest from CheckMate 77T and CheckMate 816 to make them comparable to one another based on propensity scores. [c]Sex, race, clinical stage, tumor histology, PD-L1 expression, age, ECOG PS, and smoking status. [d]Database locks: CheckMate 816, October 20, 2021; CheckMate 77T, April 26, 2024. 1. Forde PM, et al. *N Engl J Med* 2022;386:1973–1985. 2. Cascone T, et al. *N Engl J Med* 2024;390:1756–1769.

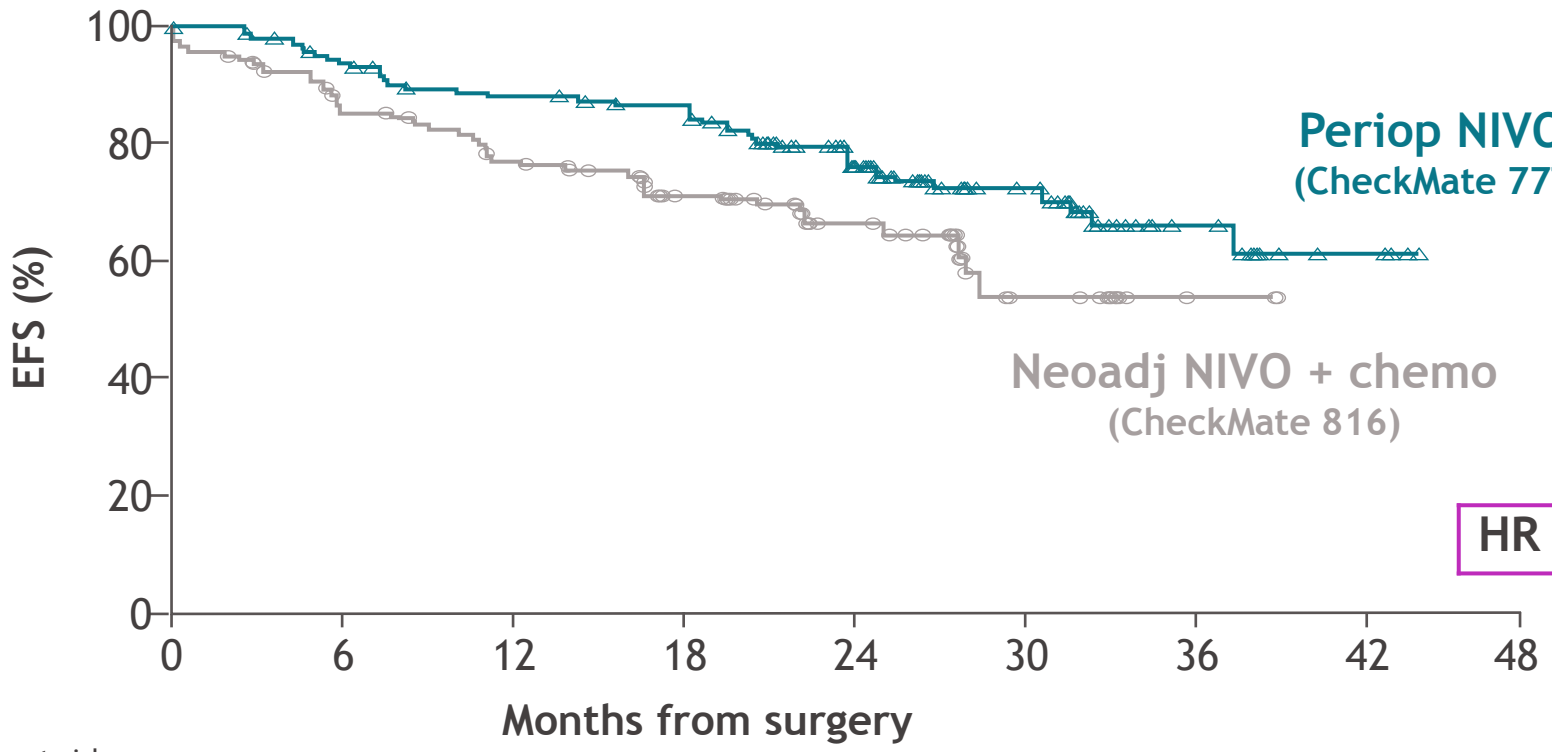
Baseline characteristics: analysis populations[a]

	Unweighted	
	Perioperative NIVO (n = 139), %	Neoadjuvant NIVO + chemo (n = 147), %
Age < 65 years	48	52
Male	73	69
Asian	27	50
ECOG PS ≥ 1	33	25
Disease stage		
Stage IB–II	35	37
Stage III non-N2	24	16
Stage III N2	40	47
Squamous NSCLC	50	46
Current/former smoker,[b]	94	90
Tumor PD-L1 expression ≥ 1%	58	50

- Baseline characteristics between patients who received perioperative NIVO or neoadjuvant NIVO + chemo were generally balanced after propensity score weighting (ATT and ATE)[c]

[a]Patients missing any variable used in propensity score computation were excluded from analyses; includes only patients with an EFS time at least up to the surgery. [b]Includes patients with unknown smoking status. [c]ATT: varying weights were applied to patients in the neoadjuvant NIVO + chemo arm (CheckMate 816) to make them comparable to those in the perioperative NIVO arm (CheckMate 77T); ATE: varying weights were applied to all patients in both neoadjuvant NIVO + chemo arm (CheckMate 816) and perioperative NIVO (CheckMate 77T) to make them comparable to one another.

Landmark EFS (BICR) from definitive surgery



No. at risk

Periop NIVO	139.4	128.0	118.1	112.9	79.7	42.5	13.0	3.1	0
Neoadj N+C	147.5	121.0	106.2	84.2	39.1	12.1	2.2	0	0

Weighted (ATE)[b]

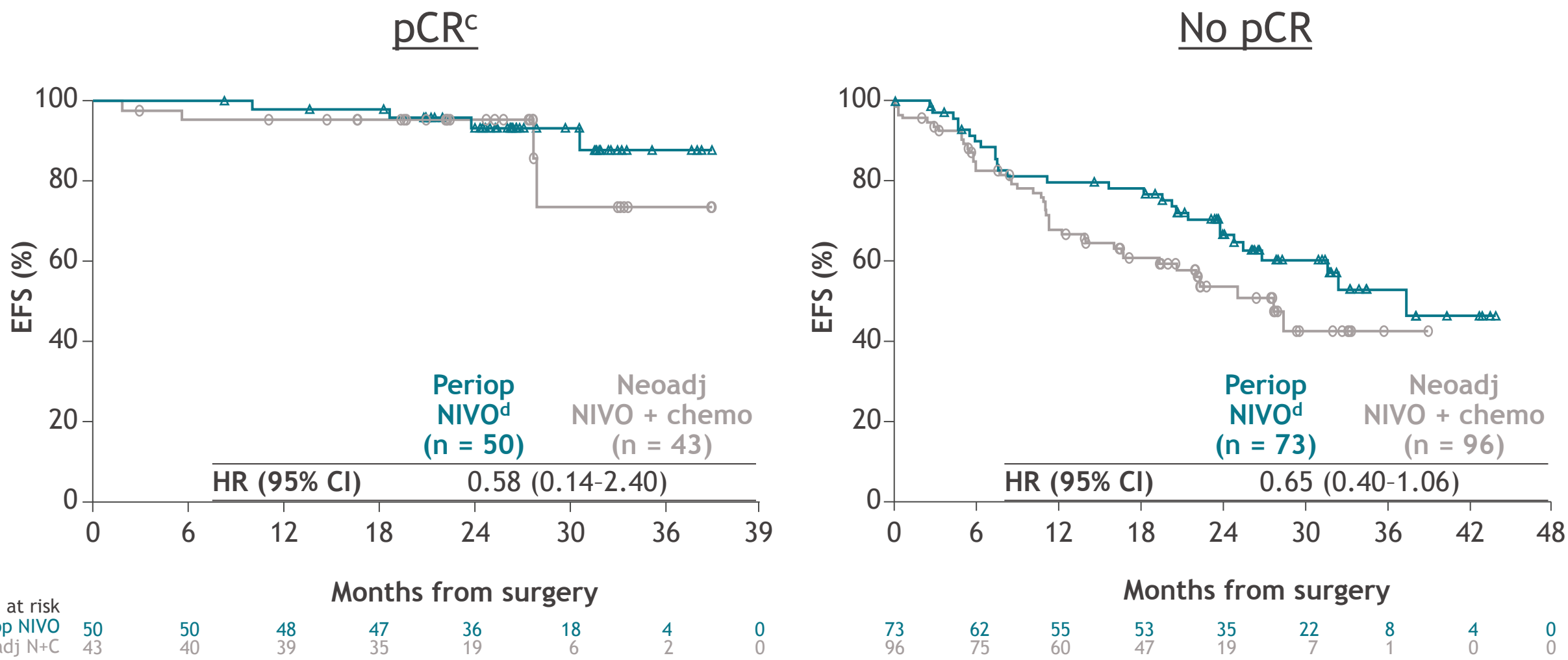
	Periop NIVO[a] (n = 139.4[c])	Neoadj NIVO + chemo (n = 147.5[c])
HR (95% CI)	0.61 (0.39-0.97)	

- HR (95% CI): ATT[d] weighted analysis, 0.56 (0.35–0.90); unweighted analysis, 0.59 (0.38–0.92)

Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [b]ATE: varying weights were applied to all patients in both neoadjuvant NIVO + chemo arm (CheckMate 816) and perioperative NIVO (CheckMate 77T) to make them comparable to one another. [c]N values fractional due to weighting. [d]ATT: varying weights were applied to patients in the neoadjuvant NIVO + chemo arm (CheckMate 816) to make them comparable to those in the perioperative NIVO arm (CheckMate 77T).

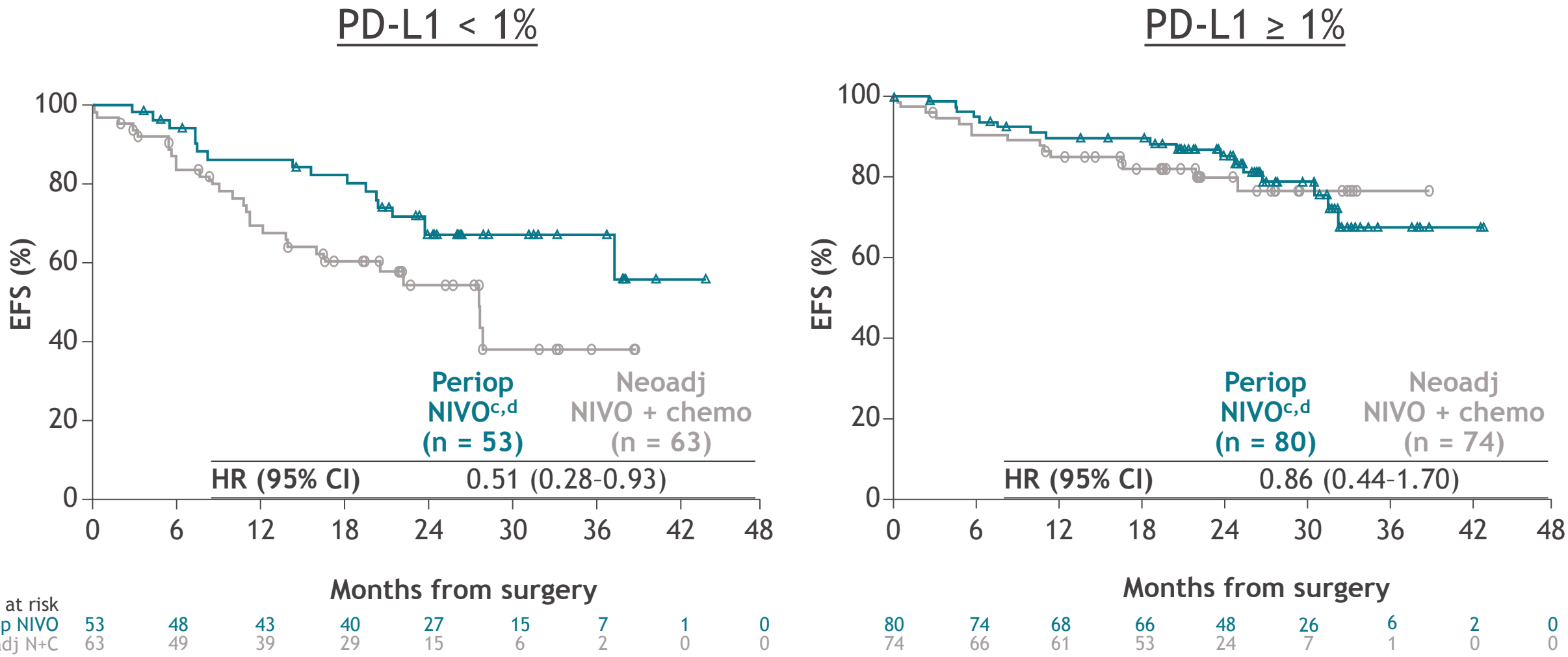
In the unweighted analysis population, 89 patients (64%) completed adjuvant therapy, and median number of doses (range) was 13.0 (1–13). Unweighted landmark EFS from surgery among all patients who had surgery (regardless of whether they received adjuvant NIVO in CheckMate 77T) for periop NIVO vs neoadj NIVO + chemo: HR = 0.82 (95% CI, 0.55–1.21).

Landmark EFS[a] (analysis population) by pCR status[a,b]



Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable pCR status were excluded. [b]Unweighted analyses.
[c]pCR rates in this analysis population: perioperative NIVO, 40.7%; neoadjuvant NIVO + chemo, 30.5%. [d]Includes only patients who received ≥ 1 dose of adjuvant NIVO.

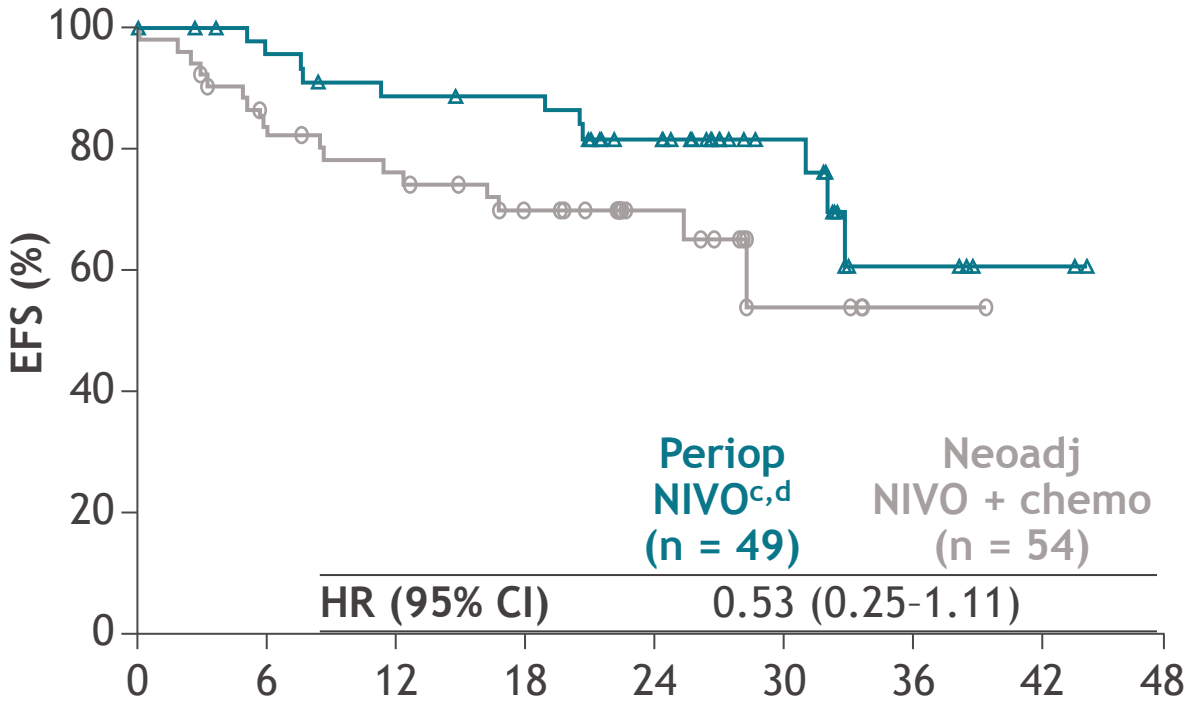
Landmark EFS (analysis population) by tumor PD-L1 expression[a,b]



Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable PD-L1 expression were excluded. [b]Unweighted analyses. [c]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [d]Completed adjuvant treatment: < 1%, 33 patients (62%) and ≥ 1%, 51 patients (64%). Median number of doses (range): < 1%, 13 (1–13) and ≥ 1%, 13 (1–13).

Landmark EFS (analysis population) by clinical stage[a,b]

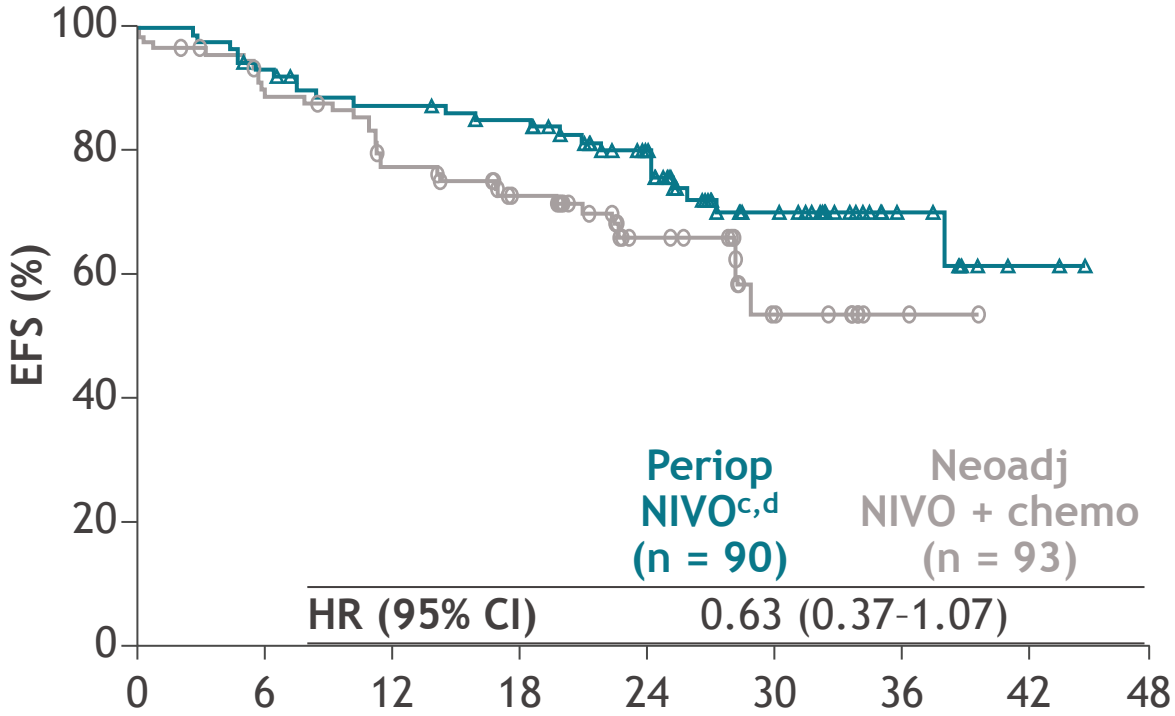
Stage IB–II



No. at risk

Periop NIVO	49	44	40	39	29	15	5	2	0
Neoadj N+C	54	42	38	31	15	4	1	0	0

Stage III



Periop NIVO	90	83	76	72	50	29	9	2	0
Neoadj N+C	93	80	68	55	26	9	2	0	0

Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with disease stage other than IB, II, III were excluded. [b]Unweighted analyses. [c]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [d]Completed adjuvant treatment: stage IB-II, 35 patients (71%) and stage III, 54 patients (60%). Median number of doses (range): stage IB-II, 13 (1-13) and stage III, 13 (1-13).

Safety summary[a]: analysis populations

Patients, n (%)	Perioperative NIVO (n = 139)		Neoadjuvant NIVO + chemo (n = 147)	
	Any grade[b]	Grade 3-4[b]	Any grade[c]	Grade 3-4[c]
All AEs	137 (99)	64 (46)	138 (94)	63 (43)
TRAEs	130 (94)	38 (27)	125 (85)	52 (35)
All AEs leading to discontinuation	29 (21)	10 (7)	16 (11)	8 (5)
TRAEs leading to discontinuation	22 (16)	9 (6)	16 (11)	8 (5)
All SAEs	57 (41)	37 (27)	23 (16)	16 (11)
Treatment-related SAEs	23 (16)	14 (10)	17 (12)	13 (9)
Surgery-related AEs[d]	53 (38)	15 (11)	61 (42)	17 (12)
Treatment-related deaths[e]	0		0	

[a]AEs per CTCAE v4.0 and MedDRA v24.0 (CheckMate 816) or v26.1 (CheckMate 77T). [b]Includes events reported between the first dose and 30 days after the last dose of study treatment. [c]Includes events reported between the first neoadjuvant dose and 30 days after the last dose of neoadjuvant study treatment. [d]Includes events reported within 90 days after definitive surgery. [e]Treatment-related deaths occurring at any time after the first dose of neoadjuvant study treatment.

Summary

- In the absence of a randomized-controlled trial, this analysis represents the only comparison of perioperative vs neoadjuvant-only immunotherapy treatments for patients with resectable NSCLC, using individual patient-level data from 2 randomized phase 3 trials
- Approximately 40% reduction in risk of disease recurrence or death after surgery was observed in patients who received ≥ 1 dose of adjuvant NIVO following neoadjuvant NIVO + chemo treatment and surgery compared with those who did not receive adjuvant NIVO
  - Similar benefit was seen regardless of baseline stage, with a greater magnitude of benefit in patients with tumor PD-L1 expression < 1%
  - Perioperative NIVO improved EFS benefit vs neoadjuvant NIVO + chemo for patients without a pCR
- Perioperative NIVO had a generally manageable safety profile
- These results help inform the potential benefit of adjuvant NIVO following neoadjuvant NIVO + chemo treatment and surgery and further support perioperative NIVO as a treatment option for eligible patients with resectable NSCLC

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We would like to acknowledge all of the investigators of the CheckMate 77T trial

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Abbreviations

AE, adverse event

ATE, average treatment effect

ATT, average treatment effect for the treated

BICR, blinded independent central review

Chemo, chemotherapy

CI, confidence interval

CTCAE, Common Terminology Criteria for Adverse Events

ECOG PS, Eastern Cooperative Oncology Group performance status

EFS, event-free survival

HR, hazard ratio

IHC, immunohistochemistry

IPTW, inverse probability of treatment weighting

MedDRA, Medical Dictionary for Regulatory Activities

mo, month

N+C, nivolumab plus chemotherapy

NIVO, nivolumab

Neoadj, neoadjuvant

NSCLC, non–small cell lung cancer

Periop, perioperative

pCR, pathological complete response

PD-L1, programmed death ligand 1

RT, radiotherapy

SAE, serious adverse event

TRAE, treatment-related adverse event

vs, versus