

# Resection and pathological response after neoadjuvant nivolumab plus chemotherapy for lung cancer in a Turkish Oncology Group (TOG) real-world study

**Erdem Sünger**

erdemsunger@gmail.com

Istanbul Medipol University, Medipol Mega University Hospital

**Bahadır Köylü**

Koç University School of Medicine

**Tuğba Akın Telli**

Demiroğlu Bilim University, Istanbul Florence Nightingale Hospital

**Hayati Arvas**

Dicle University Faculty of Medicine

**Gül Akın**

Bursa Uludağ University Faculty of Medicine

**Güneş Dorukhan Çavuşoğlu**

Çukurova University Faculty of Medicine

**Özgür Han**

University of Health Sciences, Istanbul Training and Research Hospital

**Maral Martin Mıldanoğlu**

Istanbul Medipol University, Medipol Mega University Hospital

**Tuncay Koç**

Meddem Hospital

**İsmail Bayrakçı**

Trakya University Faculty of Medicine

**Ergin Aydemir**

University of Health Sciences, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital

**Nisanur Sarıyar Busery**

University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital

**İlkay Çıttakkul**

Kocaeli University Faculty of Medicine

**Ali Kaan Güren**

Marmara University Faculty of Medicine

**Gülhan İpek Deniz**

Tansan Polyclinic

**Abdullah Sakin**

Istanbul Medipol University, Medipol Bahçelievler University Hospital

**Esra Aşık**

University of Health Sciences, Trabzon Kanuni Training and Research Hospital

**Safa Can Efil**

Ankara Bilkent City Hospital

**İrem Uğurlu**

Sakarya University Training and Research Hospital

**Elif Şahin**

Kocaeli City Hospital

**Murat Araz**

Necmettin Erbakan University Faculty of Medicine

**Teoman Şakalar**

HG Private Hospital

**Yakup Ergün**

Bower Hospital

**Atike Pınar Erdoğan**

Manisa Celal Bayar University Faculty of Medicine

**Ebru Çiçek**

Istanbul University-Cerrahpaşa

**Sakine Damla Açikel Yüksel**

Acıbadem Mehmet Ali Aydınlar University School of Medicine

**Pınar Ezgi Dama**

Dokuz Eylül University Faculty of Medicine

**Nargiz Majidova Altuntash**

VM Medical Park Maltepe Hospital

**Ayberk Bayramgil**

University of Health Sciences, Ümraniye Training and Research Hospital

**Fatma Keskin Uzundere**

Dicle University Faculty of Medicine

**Şahin Laçın**

Koç University School of Medicine

**İsmail Oğuz Kara**

Çukurova University Faculty of Medicine

**Yasin Kutlu**

Istanbul Medipol University, Medipol Mega University Hospital

**Erdem Çubukçu**

Bursa Uludağ University Faculty of Medicine

**Ömer Fatih Ölmez**

Acıbadem Mehmet Ali Aydınlar University School of Medicine

**Fatih Selçukbiricik**

Koç University School of Medicine

**Ahmet Bilici**

Istanbul Medipol University, Medipol Mega University Hospital

---

## Article

**Keywords:** Non-small cell lung cancer, Neoadjuvant chemoimmunotherapy, Nivolumab, PD-L1, Pathological complete response, Real-world evidence

**Posted Date:** October 23rd, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-11204389/v1>

**License:** © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Additional Declarations:** No competing interests reported.

---

# Abstract

Neoadjuvant nivolumab plus platinum-based chemotherapy is standard care for resectable non-small cell lung cancer, but patients who start it and never undergo resection remain poorly characterized. We retrospectively analyzed 211 consecutive patients with clinical stage IB–IIIB disease without *EGFR*, *ALK* or *ROS1* alterations who started treatment at 28 Turkish Oncology Group centers, following each patient from the first cycle. Most patients (83.9%) had stage III disease; the objective response rate was 84.4%. Resection was performed in 132 patients (62.6%); non-resected patients more often had T4 tumors (39.2% vs 15.9%). Counting non-resected patients as non-responders, pathological complete response was 24.6% and major pathological response (including complete response) 38.9%, comparable with CheckMate 816. Higher programmed death-ligand 1 expression was independently associated with major pathological response (odds ratio 2.13 per category, 95% confidence interval 1.09–4.17), whereas worsening radiological response was the only independent correlate of non-resection. Of non-resected patients, 57.0% received thoracic radiotherapy, mostly chemoradiotherapy. Immune-related adverse events occurred in 17.5% (grade 3–4, 3.8%). At a median follow-up of 15.9 months, 24-month event-free and overall survival were 63.2% and 80.0%. Pathological activity was preserved in routine practice, but more than one third of patients never reached surgery.

## Introduction

Lung cancer is the most frequently diagnosed malignancy and the leading cause of cancer death worldwide, with approximately 2.5 million new cases and 1.8 million deaths in 2022 [1]. Non-small cell lung cancer (NSCLC) accounts for 80–85% of cases, and only about one quarter of patients present with disease amenable to curative-intent local therapy [2, 3]. Recurrence nevertheless develops in roughly 30% of completely resected patients, and preoperative chemotherapy alone improves absolute 5-year survival by only about 5 percentage points while producing pathological complete response (pCR), the absence of viable tumor in the resected lung and lymph nodes, in a median of approximately 4% [2, 4].

The addition of immune checkpoint inhibitors to preoperative chemotherapy has changed this landscape, and the rationale for giving them before rather than after surgery is immunological. Blockade of programmed cell death protein 1 is delivered while the primary tumor and its draining lymph nodes are still in place, so that tumor antigen released by concurrent platinum-based chemotherapy is presented in the anatomical compartment in which tumor-specific T cell clones are primed and from which they expand systemically. The residual viable tumor in the resection specimen then provides an early, tissue-level read-out of that immune activity, and has been evaluated as a surrogate for event-free survival (EFS) [5]. In the phase 3 CheckMate 816 trial, neoadjuvant nivolumab plus chemotherapy improved EFS and pCR (24.0% vs 2.2%) and, on mature analysis, overall survival (OS), with a hazard ratio of 0.72 and a 95% confidence interval (CI) of 0.52–0.998 [6, 7]. Perioperative regimens in the NADIM II, KEYNOTE-671, AEGEAN, CheckMate 77T and NEOTORCH trials reproduced these pathological and survival advantages [2, 8–12]. Because checkpoint inhibitors have limited activity in *EGFR*-mutant or *ALK*-rearranged disease,

where adjuvant targeted therapy is preferred, the expected benefit applies chiefly to tumors without these alterations [13–15].

Translating this evidence into routine care has proved less straightforward than the trials suggest [16]. Trial participants are younger, fitter and less comorbid than patients treated in practice, and trials restrict analysis to those considered resectable at baseline. Patients who begin neoadjuvant treatment but do not proceed to resection therefore remain incompletely characterized, particularly regarding subsequent management and outcomes: about 17% of patients in CheckMate 816 and 19% in AEGEAN did not undergo planned surgery [6, 11], and the proportion reaching resection varies widely in routine practice – 78% in a three-center United States cohort [17], 87.5% in a prospective Czech nationwide series [18] and 91.3% in a 29-center Japanese cohort [19]. A recent dedicated analysis has begun to characterize patients who do not proceed to surgery [19], but contemporary non-resected cohorts remain small, limiting characterization of their real-world treatment trajectories.

We therefore analyzed a national, 28-center Turkish Oncology Group cohort of consecutive patients with clinical stage IB–IIIB NSCLC without *EGFR*, *ALK* or *ROS1* alterations who started neoadjuvant platinum-based chemotherapy plus nivolumab. Rather than restricting analysis to the resected subset, we followed the entire treated population from the first neoadjuvant cycle onward, reporting pathological response on an intention-to-treat (ITT) basis, in which non-resected patients are counted as non-responders, and describing the subsequent management and early outcomes of patients who never reached resection.

## Results

### Patient characteristics

A total of 211 patients treated at 28 centers were included (Fig. 1; Table 1). The median age was 64 years (range 34–84 years); 75.8% were male and 94.8% were current or former smokers. Baseline Eastern Cooperative Oncology Group performance status (ECOG PS) was 0 in 62.6% and 1 in 36.5%. Squamous cell carcinoma was the most frequent histology (55.0%), followed by adenocarcinoma (41.2%). The cohort was predominantly locally advanced: 177 patients (83.9%) had stage III disease (IIIA 55.9%, IIIB 28.0%), 121 (57.4%) had clinical N2 or N3 involvement and 52 (24.6%) had T4 tumors. The programmed death-ligand 1 (PD-L1) tumor proportion score was less than 1% in 20.9%, 1–49% in 39.3%, 50% or greater in 22.7% and unknown in 17.1%. Comorbidity was present in 64.9%.

Table 1

Baseline demographic and clinicopathological characteristics of the overall cohort and according to whether resection was performed.

| Characteristic              | Overall cohort<br>(N = 211) | Resected<br>(n = 132) | Not resected<br>(n = 79) | p value |
|-----------------------------|-----------------------------|-----------------------|--------------------------|---------|
| Age, median (range), years  | 64 (34–84)                  | 64 (44–84)            | 63 (34–80)               | 0.99    |
| Age, mean $\pm$ s.d., years | 63.2 $\pm$ 9.0              | 63.3 $\pm$ 8.3        | 63.1 $\pm$ 10.1          |         |
| <b>Sex</b>                  |                             |                       |                          | 0.76    |
| Male                        | 160 (75.8)                  | 101 (76.5)            | 59 (74.7)                |         |
| Female                      | 51 (24.2)                   | 31 (23.5)             | 20 (25.3)                |         |
| <b>Smoking history</b>      |                             |                       |                          | 0.80    |
| Never                       | 11 (5.2)                    | 6 (4.5)               | 5 (6.3)                  |         |
| Former                      | 114 (54.0)                  | 73 (55.3)             | 41 (51.9)                |         |
| Current                     | 86 (40.8)                   | 53 (40.2)             | 33 (41.8)                |         |
| <b>ECOG PS</b>              |                             |                       |                          | 0.10    |
| 0                           | 132 (62.6)                  | 87 (65.9)             | 45 (57.0)                |         |
| 1                           | 77 (36.5)                   | 45 (34.1)             | 32 (40.5)                |         |
| 2                           | 2 (0.9)                     | 0 (0.0)               | 2 (2.5)                  |         |
| <b>Clinical T stage</b>     |                             |                       |                          | 0.003   |
| T1                          | 20 (9.5)                    | 14 (10.6)             | 6 (7.6)                  |         |
| T2                          | 69 (32.7)                   | 51 (38.6)             | 18 (22.8)                |         |
| T3                          | 70 (33.2)                   | 46 (34.8)             | 24 (30.4)                |         |
| T4                          | 52 (24.6)                   | 21 (15.9)             | 31 (39.2)                |         |
| <b>Clinical N stage</b>     |                             |                       |                          | 0.39    |
| N0                          | 35 (16.6)                   | 18 (13.6)             | 17 (21.5)                |         |
| N1                          | 55 (26.1)                   | 37 (28.0)             | 18 (22.8)                |         |

Data are n (%) unless otherwise stated. The p values were calculated with the Pearson chi-square test for categorical variables and the Mann–Whitney U test for age; all tests were two-sided. The chi-square test for clinical T stage used the original detailed categories (T1b–T4). The PD-L1 chi-square test was restricted to patients with a known result (resected, n = 109; not resected, n = 66).

ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; s.d., standard deviation; TPS, tumor proportion score.

| Characteristic                                                                                                                                                                                                                                                                                                                                                                                              | Overall cohort<br>(N = 211) | Resected<br>(n = 132) | Not resected<br>(n = 79) | p value |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------|--------------------------|---------|
| N2                                                                                                                                                                                                                                                                                                                                                                                                          | 116 (55.0)                  | 73 (55.3)             | 43 (54.4)                |         |
| N3                                                                                                                                                                                                                                                                                                                                                                                                          | 5 (2.4)                     | 4 (3.0)               | 1 (1.3)                  |         |
| <b>Clinical stage</b>                                                                                                                                                                                                                                                                                                                                                                                       |                             |                       |                          | 0.38    |
| IB                                                                                                                                                                                                                                                                                                                                                                                                          | 5 (2.4)                     | 3 (2.3)               | 2 (2.5)                  |         |
| IIA                                                                                                                                                                                                                                                                                                                                                                                                         | 4 (1.9)                     | 4 (3.0)               | 0 (0.0)                  |         |
| IIB                                                                                                                                                                                                                                                                                                                                                                                                         | 25 (11.8)                   | 18 (13.6)             | 7 (8.9)                  |         |
| IIIA                                                                                                                                                                                                                                                                                                                                                                                                        | 118 (55.9)                  | 74 (56.1)             | 44 (55.7)                |         |
| IIIB                                                                                                                                                                                                                                                                                                                                                                                                        | 59 (28.0)                   | 33 (25.0)             | 26 (32.9)                |         |
| <b>Histology</b>                                                                                                                                                                                                                                                                                                                                                                                            |                             |                       |                          | 0.24    |
| Squamous cell carcinoma                                                                                                                                                                                                                                                                                                                                                                                     | 116 (55.0)                  | 68 (51.5)             | 48 (60.8)                |         |
| Adenocarcinoma                                                                                                                                                                                                                                                                                                                                                                                              | 87 (41.2)                   | 60 (45.5)             | 27 (34.2)                |         |
| Other                                                                                                                                                                                                                                                                                                                                                                                                       | 8 (3.8)                     | 4 (3.0)               | 4 (5.1)                  |         |
| <b>PD-L1 TPS</b>                                                                                                                                                                                                                                                                                                                                                                                            |                             |                       |                          | 0.82    |
| < 1%                                                                                                                                                                                                                                                                                                                                                                                                        | 44 (20.9)                   | 29 (22.0)             | 15 (19.0)                |         |
| 1–49%                                                                                                                                                                                                                                                                                                                                                                                                       | 83 (39.3)                   | 50 (37.9)             | 33 (41.8)                |         |
| ≥ 50%                                                                                                                                                                                                                                                                                                                                                                                                       | 48 (22.7)                   | 30 (22.7)             | 18 (22.8)                |         |
| Unknown                                                                                                                                                                                                                                                                                                                                                                                                     | 36 (17.1)                   | 23 (17.4)             | 13 (16.5)                |         |
| Comorbidity present                                                                                                                                                                                                                                                                                                                                                                                         | 137 (64.9)                  | 85 (64.4)             | 52 (65.8)                | 0.83    |
| Data are n (%) unless otherwise stated. The p values were calculated with the Pearson chi-square test for categorical variables and the Mann–Whitney U test for age; all tests were two-sided. The chi-square test for clinical T stage used the original detailed categories (T1b–T4). The PD-L1 chi-square test was restricted to patients with a known result (resected, n = 109; not resected, n = 66). |                             |                       |                          |         |
| ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; s.d., standard deviation; TPS, tumor proportion score.                                                                                                                                                                                                                                                    |                             |                       |                          |         |

After neoadjuvant therapy, 132 patients (62.6%) underwent resection and 79 (37.4%) did not. The two groups were similar in age, sex, smoking history, ECOG PS, comorbidity, clinical N stage, overall stage, histology and PD-L1 expression (all  $p > 0.05$ ; Table 1). They differed in clinical T stage (chi-square test,  $p = 0.003$ ): T4 disease was present in 31 of 79 non-resected patients (39.2%) compared with 21 of 132 resected patients (15.9%).

## Treatment and response

The neoadjuvant regimen was carboplatin, paclitaxel and nivolumab in 192 patients (91.0%), cisplatin, gemcitabine and nivolumab in 16 (7.6%), and cisplatin, pemetrexed and nivolumab in 3 (1.4%). The median number of chemotherapy cycles was 4 (range 2–6) and of nivolumab cycles 3 (Supplementary Table S1).

The objective response rate, defined as complete or partial response according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, was 84.4% (178 of 211), comprising complete response in 36 patients (17.1%) and partial response in 142 (67.3%); stable disease and progressive disease occurred in 10.0% and 5.7%, respectively (Supplementary Fig. S1). Among the 132 resected patients, lobectomy was performed in 108 (81.8%), pneumonectomy in 20 (15.2%) and segmentectomy in 4 (3.0%). A pCR was observed in 52 (39.4%) and a major pathological response (MPR; 10% or less residual viable tumor), including pCR, in 82 (62.1%). Absence of nodal metastasis after neoadjuvant therapy (ypN0) was recorded in 94 patients (71.2%), although 18 of these had been clinically node-negative at baseline, so nodal clearance from a node-positive baseline was documented in 76 patients. Across the whole treated cohort on an ITT basis, pCR was 24.6% and MPR 38.9%. The pCR rate was numerically higher with squamous than adenocarcinoma histology (49% vs 32%) and rose with PD-L1 expression (28%, 32% and 53% for less than 1%, 1–49% and 50% or greater, respectively; Supplementary Fig. S1).

## Management after neoadjuvant therapy

Post-neoadjuvant management differed substantially according to whether resection was achieved (Table 2). Among the 132 resected patients, 73 (55.3%) received adjuvant or consolidation therapy, most often immunotherapy alone (31.1%) or immunotherapy with radiotherapy (9.8%); in total, 63 (47.7%) received a regimen containing a checkpoint inhibitor, and 19 (14.4%) received postoperative radiotherapy.

Table 2

Management after neoadjuvant therapy and clinical outcomes according to whether resection was performed.

| Variable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Resected (n = 132) | Not resected (n = 79) |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------|
| Any subsequent antineoplastic therapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 73 (55.3)          | 47 (59.5)             |
| No further therapy recorded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 59 (44.7)          | 32 (40.5)             |
| <b>Type of subsequent therapy</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                    |                       |
| Immunotherapy alone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 41 (31.1)          | 2 (2.5)               |
| Immunotherapy plus radiotherapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 13 (9.8)           | 12 (15.2)             |
| Chemotherapy alone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 8 (6.1)            | 0 (0.0)               |
| Chemotherapy plus immunotherapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 5 (3.8)            | 0 (0.0)               |
| Chemoradiotherapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1 (0.8)            | 30 (38.0)             |
| Chemotherapy, immunotherapy and radiotherapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 4 (3.0)            | 1 (1.3)               |
| Other radiotherapy-containing regimen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 1 (0.8)            | 2 (2.5)               |
| Any thoracic radiotherapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 19 (14.4)          | 45 (57.0)             |
| <b>Clinical outcomes</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                    |                       |
| Recurrence or progression                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 25 (18.9)          | 23 (29.1)             |
| Death from any cause                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 13 (9.8)           | 15 (19.0)             |
| 12-month EFS, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 93                 | 72                    |
| 24-month EFS, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 71                 | 50                    |
| 12-month OS, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 95                 | 82                    |
| 24-month OS, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 86                 | 69                    |
| Data are n (%) unless otherwise stated. Percentages are calculated within each column denominator (resected, n = 132; not resected, n = 79). Among resected patients, regimens containing a checkpoint inhibitor (immunotherapy alone, immunotherapy plus radiotherapy, chemotherapy plus immunotherapy, and chemotherapy with immunotherapy and radiotherapy) were received by 63 patients (47.7%). Radiotherapy-containing regimens include chemoradiotherapy, radiotherapy with immunotherapy and other combinations incorporating thoracic radiotherapy; individual patients are counted once according to the recorded regimen. The curative or palliative intent of radiotherapy was not recorded. "No further therapy recorded" denotes the absence of a documented subsequent antineoplastic treatment in the database and does not necessarily indicate that no treatment was given. Survival percentages are Kaplan–Meier estimates. |                    |                       |
| EFS, event-free survival; OS, overall survival.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                    |                       |

Among the 79 patients who did not undergo resection, 47 (59.5%) had further antineoplastic therapy recorded and 45 (57.0%) received thoracic radiotherapy. The most frequent approach was

chemoradiotherapy (30 patients, 38.0%), followed by radiotherapy with immunotherapy (12, 15.2%); 3 (3.8%) received other radiotherapy-containing regimens and 2 (2.5%) systemic therapy alone. For 32 (40.5%), no subsequent treatment was recorded. The intent of radiotherapy was not captured, so curative and palliative courses cannot be distinguished, and the reasons for not proceeding to resection were not recorded in a structured field.

## Safety

Immune-related adverse events (irAEs) of any grade occurred in 37 patients (17.5%) and grade 3 or 4 events in 8 (3.8%). The most frequent were hypothyroidism (5.2%), interstitial lung disease (2.4%) and colitis (1.9%); the full distribution is given in Supplementary Table S2. The occurrence of an irAE was not associated with EFS (log-rank  $p = 0.32$ ) or OS (log-rank  $p = 0.39$ ). Whether an irAE delayed or prevented surgery was not recorded.

## Survival

Median follow-up by the reverse Kaplan–Meier method was 15.9 months. Recurrence after resection occurred in 25 of 132 patients (18.9%) and progression among non-resected patients in 23 of 79 (29.1%), giving 48 EFS events (22.7%); 28 patients (13.3%) died, 13 (9.8%) resected and 15 (19.0%) non-resected.

In the whole cohort, 12- and 24-month EFS were 85.4% and 63.2%, and OS 90.1% and 80.0% (Fig. 2). Because only 33 patients remained at risk for EFS and 42 for OS at 24 months, estimates beyond 24 months are not reported.

EFS and OS were longer in resected than non-resected patients, with 24-month EFS of 71% versus 50% and 24-month OS of 86% versus 69% (log-rank  $p = 0.004$  and  $p = 0.011$ , respectively; Fig. 3). These crude comparisons are subject to selection and guarantee-time bias, because resection is a post-baseline outcome conditional on treatment response, clinical fitness and survival to surgery, and non-resected patients also more often had T4 disease at baseline; they should therefore not be interpreted as estimating the causal effect of surgery.

Radiological response separated the survival curves strongly (log-rank  $p < 0.001$  for both endpoints; Supplementary Fig. S2), and depth of pathological response was associated with EFS and OS in the resected cohort (log-rank  $p < 0.001$  and  $p = 0.018$ , respectively; Fig. 4): patients achieving pCR had 24-month EFS of 96% and OS of 98%, compared with 24-month EFS of 80% with MPR without pCR and 44% without MPR. Because few patients in the MPR without pCR group remained at risk late in follow-up (10 at 24 months and 1 at 36 months), the late crossing of the OS curves in that group reflects a single event and is not interpretable. Higher PD-L1 expression was associated with EFS (24-month EFS 81% for  $\geq 50\%$  vs 49% for  $< 1\%$ ; log-rank  $p = 0.023$ ; Fig. 5a) but not with OS (log-rank  $p = 0.96$ ). EFS according to three-level clinical stage group is shown in Fig. 5b (log-rank  $p = 0.100$ ); with the five-level stage classification,

EFS differed across stages (log-rank  $p < 0.001$ ), and three-level stage was associated with OS (log-rank  $p = 0.024$ ). Univariable log-rank comparisons for all baseline, treatment and pathological variables are summarized in Supplementary Table S3.

## Factors associated with pathological response and with resection

In resected patients, multivariable logistic regression ( $n = 109$ ; Nagelkerke  $R^2 = 0.337$ ) associated higher PD-L1 expression with MPR, including pCR, with an odds ratio (OR) of 2.13 per category (95% CI 1.09–4.17;  $p = 0.027$ ), whereas each one-category worsening of radiological response was associated with markedly lower odds (OR 0.08, 95% CI 0.02–0.31;  $p < 0.001$ ; Fig. 6a). A nominal association with ECOG PS (OR 2.90, 95% CI 1.01–8.34;  $p = 0.048$ ) is biologically counterintuitive, borders the significance threshold and most likely reflects model instability. Clinical T, N and overall stage were not associated with pathological response.

In the whole cohort, the only independent correlate of undergoing resection was post-neoadjuvant radiological response ( $n = 172$ ; Nagelkerke  $R^2 = 0.178$ ): each one-category worsening of response was associated with lower odds of resection (OR 0.36, 95% CI 0.20–0.65;  $p = 0.001$ ; Fig. 6b). Clinical T stage, which differed between resected and non-resected patients (Table 1), and overall clinical stage were not independently associated with resection, so in this exploratory model radiological response showed a stronger association with resection than baseline stage.

## Discussion

In this national cohort of 211 consecutive patients treated at 28 centers, neoadjuvant nivolumab plus platinum-based chemotherapy produced an objective response rate of 84.4% and an ITT pCR rate of 24.6% in a population in which 83.9% had stage III disease. Immune-related toxicity was infrequent, while survival estimates remain early because of limited follow-up. The defining feature of the cohort is that more than one third of patients never reached the operating room, and that their subsequent management and outcomes were captured rather than excluded.

Reporting pathological response on an ITT basis is essential here. Within our resected cohort, pCR reached 39.4% and MPR 62.1%, exceeding the National Cancer Database (pCR 30.2%) [3] and a European surgical series (pCR 30%; MPR 52.7%) [20], and matching another real-world nivolumab series (combined pCR and MPR 61%) [21]. Such figures are inflated by the selection of good responders into surgery. Computed across all treated patients, our ITT pCR of 24.6% aligns closely with CheckMate 816 (24.0%) [6] and exceeds the 17% reported by Cooper and colleagues on the same intention-to-treat principle [17]. Because both denominators include patients who never reached resection, this comparison suggests that the pathological activity of chemoimmunotherapy is preserved despite a more advanced case mix.

The proportion of patients proceeding to surgery nonetheless varies considerably across real-world cohorts. Our resection rate of 62.6% is lower than the 78% observed by Cooper et al. [17], the 76.9% reported in a Chinese single-center series of potentially resectable stage III disease [22], the 81–83% in CheckMate 816 and AEGEAN [6, 11], the 87.5% in a prospective Czech nationwide series [18] and the 91.3% in a 29-center Japanese cohort [19]. These differences may partly reflect variation in case mix, baseline resectability and local multidisciplinary selection: stage III disease accounted for 63% of the United States and 68.8% of the Czech cohort but 83.9% of ours, the Czech series was confined to PD-L1-positive stage IIB–IIIB disease, and T4 tumors were substantially more common among our non-resected than resected patients (39.2% vs 15.9%). Reported correlates of attrition also differ: older age in the United States series [17], and disease progression, patient refusal and irAEs in the Japanese analysis [19]. In our cohort, radiological response after induction was the only variable independently associated with resection. Together these observations suggest that attrition before surgery reflects a combination of case mix, treatment response, toxicity, resectability assessment, patient preference and local care pathways.

For most non-resected patients, not proceeding to resection did not mean the end of active anticancer treatment: 57.0% received thoracic radiotherapy, most often as chemoradiotherapy, and the 24-month OS of the non-resected group was 69%. Because the intent of radiotherapy was not recorded, we cannot state how many courses were radical. Radiotherapy-based local treatment has also been reported in other contemporary series of patients unable to undergo planned surgery: six of eight non-resected patients received radiotherapy in the Czech series [18]; all 45 patients who did not reach surgery received radiotherapy-based salvage treatment in the Chinese series [22]; whereas in the Japanese analysis only 36% of 11 non-resected patients received intensive salvage treatment and 36% best supportive care [19]. A prospective German cohort similarly reported that most patients not reaching resection proceeded to chemoradiotherapy [23], and dedicated series have examined definitive radiotherapy after planned neoadjuvant chemoimmunotherapy [24] and compared chemoradiotherapy with surgery in this setting [25]. Chemoradiotherapy with consolidation immunotherapy is the established approach in unresected stage III disease [26], although our design permits no direct comparison. With 79 non-resected patients, this cohort is among the larger contemporary series in which this trajectory has been described.

Early markers of immune activity behaved consistently across independent analyses. PD-L1 expression was independently associated with pathological response in our cohort (OR 2.13 per category), as it was in the United States series (OR 12.1 for expression of 50% or greater vs negative) [17], and was also associated with EFS in univariable analysis. It should not, however, be used to withhold therapy, because meta-analysis demonstrates EFS benefit even in PD-L1-negative disease [27]. Radiological response was associated both with pathological response and with the probability of resection, making it an accessible early signal, although assessment was local and radiological–pathological discordance is well recognized after immunotherapy. The pCR rate was higher in squamous than adenocarcinoma histology (49% vs 32%), as in European and Czech series (39% vs 23% and 66.7% vs 27.6%) [18, 20], but histology was not associated with survival here.

Read immunologically, these observations are compatible with the mechanism proposed for the neoadjuvant sequence, in which checkpoint blockade acts on an intact tumor–lymph node axis and the resection specimen serves as a pharmacodynamic read-out of the resulting antitumor immune response. Two features of our data qualify that picture. First, although PD-L1 was the only pretreatment tumor biomarker independently associated with MPR, its effect size was modest (OR 2.13 per category) and 28% of resected patients with PD-L1-negative tumors nevertheless achieved pCR, indicating that tumor cell PD-L1 captures only part of the biology that determines response; tumor mutational burden, tumor-infiltrating lymphocyte density, tertiary lymphoid structures and circulating tumor DNA clearance are candidate complementary markers that were not available in this routine-care dataset. Second, PD-L1 was associated with EFS but not with OS, and radiological response showed a stronger association with reaching surgery than any baseline variable, including PD-L1 — so the most informative read-outs in practice were dynamic rather than static. Prospective real-world cohorts that couple pathological response with serial immune monitoring would help to distinguish tumors in which chemoimmunotherapy fails to prime an effective response from those in which an effective response is generated but the patient is nonetheless lost to surgery.

Immune toxicity was infrequent and did not appear to shape outcomes: irAEs occurred in 17.5% of patients and were grade 3–4 in 3.8%, with hypothyroidism, interstitial lung disease and colitis predominating, and were associated with neither EFS nor OS. This profile is compatible with the safety experience of the pivotal neoadjuvant and perioperative nivolumab trials [6, 12] and argues against toxicity as a dominant driver of attrition in our cohort, although the case report form did not record whether an irAE delayed or prevented surgery — a mechanism that was prominent in the Japanese analysis, in which severe irAEs were far more frequent among patients whose surgery was canceled (36.4% vs 7.0%) [19]. The short duration of preoperative exposure plausibly limits both cumulative immune toxicity and the value of irAEs as a pharmacodynamic marker of benefit in this setting, in contrast with what has been described with prolonged treatment of advanced disease. After resection, 47.7% of patients received an adjuvant or consolidation regimen containing a checkpoint inhibitor, a practice whose added value after neoadjuvant chemoimmunotherapy remains uncertain and has recently been examined directly in a two-center real-world analysis [28].

Survival data must be interpreted with restraint. At a median follow-up of 15.9 months, with 48 EFS events and 28 deaths, only 24-month estimates are supportable; median EFS and later estimates are not reported. The graded relationship between depth of pathological response and EFS is nonetheless consistent with the established surrogate value of pCR and MPR [5, 7] and with mature CheckMate 816 data showing 5-year OS of 95.3% after pCR [7].

This study is large for a real-world neoadjuvant series, national in scope and treated with a near-uniform regimen, with 91.0% receiving carboplatin, paclitaxel and nivolumab — unusual homogeneity for a real-world cohort, in which several checkpoint inhibitors are typically pooled. Its limitations are equally clear. The design is retrospective and single-arm, without a comparator, and resectability was judged locally, so the cohort spans clearly resectable to potentially resectable disease. PD-L1 was tested locally with more

than one validated antibody clone, introducing potential inter-assay heterogeneity. Molecular selection was confined to *EGFR*, *ALK* and *ROS1*, and no tumor immune-microenvironment correlates (tumor mutational burden, tumor-infiltrating lymphocytes) or circulating tumor DNA were available, so biological determinants of response could not be explored beyond PD-L1. Time-to-event endpoints were anchored at diagnosis rather than treatment initiation; although the diagnosis-to-treatment interval was generally short, this limits direct comparison of absolute survival estimates with clinical trials. Follow-up is short and OS immature, responses were not centrally reviewed, the extent of nodal dissection was not verified, and margin status was unavailable. Most importantly, the reasons for not proceeding to resection, the intent of subsequent radiotherapy and whether an irAE prevented surgery were not captured in structured fields. We can describe what non-resected patients received and how they fared, but not why surgery was forgone in each case – a gap that prospective registries with predefined attrition fields should close.

In conclusion, in a predominantly stage III national cohort, neoadjuvant nivolumab plus platinum-based chemotherapy achieved ITT pathological response rates comparable with pivotal trials, with acceptable immune-related toxicity, and PD-L1 expression retained its association with pathological response and EFS in routine practice. More than one third of patients who began treatment with curative intent did not reach resection; most were managed with radiotherapy-based approaches and had lower early survival estimates than patients who underwent resection, and the non-resected group also had a higher prevalence of T4 disease. Characterizing and reducing this attrition – rather than further confirming pathological activity – is the most useful next step for real-world research in this setting. Longer follow-up is required before survival conclusions can be drawn.

## Methods

### Study design and patients

This retrospective, multicenter cohort study was conducted across 28 medical oncology centers in Türkiye under the Turkish Oncology Group and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Eligible patients had histologically confirmed clinical stage IB–IIIB NSCLC without *EGFR*, *ALK* or *ROS1* alterations and had received at least one cycle of platinum-based chemotherapy plus nivolumab with curative intent. All consecutive patients meeting these criteria at each participating center were identified from institutional records; no sampling was applied.

The study period extended from the diagnosis of the first patient on September 1, 2021 to the data cut-off on April 12, 2026. Patients were diagnosed between September 1, 2021 and January 6, 2026 and received their first cycle of neoadjuvant chemoimmunotherapy between October 15, 2021 and January 28, 2026; the last resection in the cohort was performed on February 23, 2026. April 12, 2026 was the date of the most recent recorded patient contact and served as the common censoring date for all time-to-event analyses, giving a median follow-up of 15.9 months.

# Ethics approval and consent to participate

The protocol was reviewed and approved unanimously by the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Istanbul, Türkiye) on November 13, 2025 (approval number 1355; official document reference E-10840098-202.3.02-7835, issued on November 20, 2025). The approval was granted for the study as a national, multicenter project of the Turkish Oncology Group and covered all 28 participating centers; no additional independent review board approval was obtained at individual centers, and each center contributed data only for its own patients. All methods were performed in accordance with the relevant guidelines and regulations and with the principles of the Declaration of Helsinki [29].

Individual informed consent for participation was not obtained, either in written or in verbal form. The protocol approved by the ethics committee contained no informed consent procedure, and the committee approved the study without requiring individual consent because it was a retrospective, non-interventional analysis of information that had already been generated during routine clinical care: no study-specific intervention, investigation or change to treatment was undertaken, and there was no contact with patients at any stage. Seeking individual consent retrospectively would also have introduced selection bias into a consecutive cohort in which 28 patients had died before the analysis. All participants were adults at the time of diagnosis (age range 34–84 years); no minors were included, so no parental or guardian consent was applicable. Records were abstracted locally by the treating oncologist at each center, and all data are analyzed and reported in aggregate, with no information by which an individual patient could be identified.

## Data collection and definitions

Data were abstracted from medical records into a standardized case report form by the treating oncologist at each center. Recorded variables comprised demographics, smoking history, comorbidity, ECOG PS, histology, clinical and pathological stage, PD-L1 tumor proportion score, neoadjuvant regimen and cycle number, radiological response, surgical status and procedure, pathological response, subsequent therapy, irAEs, recurrence or progression, and vital status. Comorbidity was recorded as present when at least one chronic condition from a predefined checklist (hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, hyperlipidemia, or chronic cardiac, renal, thyroid or autoimmune disease) was documented at baseline.

Molecular eligibility was defined by the absence of *EGFR*, *ALK* and *ROS1* alterations, tested locally as part of routine care; other actionable alterations were not systematically assessed. Baseline resectability was determined by each center's multidisciplinary team and encompassed clearly resectable, borderline-resectable and locally advanced potentially resectable disease, without central adjudication; the same team reassessed surgical eligibility after neoadjuvant therapy. Anatomical resection with systematic

mediastinal lymph node dissection or sampling was the institutional standard, but the extent of nodal assessment was not centrally verified.

## Treatment

All patients received nivolumab with a platinum doublet, planned for three to four cycles; regimen selection, cycle number and dose modification followed physician discretion. Doses were determined locally but were generally consistent with pivotal and real-world studies: nivolumab 360 mg every 3 weeks with carboplatin (area under the concentration–time curve 5–6) plus paclitaxel, cisplatin plus gemcitabine, or cisplatin plus pemetrexed at standard doses [2,6,21].

Patients considered unsuitable for resection after neoadjuvant therapy, or who declined surgery, continued treatment according to local practice, including chemoradiotherapy, radiotherapy with immunotherapy, or systemic therapy. The intent of radiotherapy was not captured in the case report form. Adjuvant or consolidation therapy after resection was likewise determined by physician discretion.

## Endpoints and response assessment

Radiological response was based on the local radiological assessment recorded according to RECIST version 1.1 in routine clinical practice, using imaging obtained before and after neoadjuvant therapy [30]; responses were not centrally reviewed. The objective response rate was the proportion of patients with complete or partial response. Pathological response was assessed locally according to International Association for the Study of Lung Cancer recommendations, with MPR defined as 10% or less residual viable tumor and pCR as no viable tumor (ypT0N0) [31]. Because pathological response is measurable only after resection, it was reported both within the resected cohort and, as the primary comparative measure, on an ITT basis across all 211 patients, counting non-resected patients as non-responders. Because some patients were node-negative at baseline, ypN0 reflects postoperative nodal negativity rather than downstaging in every case. Clinical stage was assigned according to the eighth edition of the TNM classification [32].

PD-L1 expression was assessed locally by immunohistochemistry using validated clones (most often 22C3, followed by SP263 and SP142) and categorized as less than 1%, 1–49%, or 50% or greater; tumors without a result were classified as unknown. EFS was measured from diagnosis to progression precluding surgery, recurrence or progression after local therapy, or death from any cause, and OS from diagnosis to death from any cause. Diagnosis was chosen as the time origin because it was the most uniformly recorded date across centers. Grading of irAEs followed the Common Terminology Criteria for Adverse Events version 5.0 [33].

## Statistical analysis

Analyses were performed with IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA; <https://www.ibm.com/products/spss-statistics>). Continuous variables are summarized as median (range), with age additionally presented as mean  $\pm$  standard deviation (s.d.), and categorical variables as counts and percentages. No sample size calculation was performed; the cohort comprised all eligible consecutive patients. Categorical variables were compared with the Pearson chi-square test and continuous variables with the Mann–Whitney U test, a non-parametric test that does not assume normally distributed data; because some categories contained few patients, chi-square p values for these variables should be regarded as approximate. Survival was estimated by the Kaplan–Meier method and reported at 12 and 24 months; median follow-up was computed by the reverse Kaplan–Meier method. Because median follow-up was 15.9 months, estimates beyond 24 months rest on few patients at risk and are not interpreted. Univariable survival comparisons used the log-rank test. Comparisons according to eventual resection status were descriptive and were not intended to estimate the causal effect of surgery, because resection is a post-baseline outcome and such comparisons are susceptible to selection and guarantee-time bias.

Factors associated with pathological response (MPR, including pCR) among resected patients and with resection in the whole cohort were examined with separate binary logistic regression models including clinically selected covariates: sex, ECOG PS, clinical T stage, clinical N stage, clinical stage, PD-L1 expression and radiological response in the pathological response model, and clinical T stage, clinical N stage, clinical stage, PD-L1 expression and radiological response in the resection model. Results are reported as ORs with 95% CIs, and p values were derived from Wald tests. Ordinal covariates were entered as ordered scores, so each OR expresses the change per one-category increment under an assumed monotonic effect, and radiological response is coded in the direction of worsening response in both models. Each model was fitted on patients with complete data for all of its covariates (n = 109 for pathological response and n = 172 for resection), and overall fit is summarized by the Nagelkerke R<sup>2</sup>. Multivariable time-to-event models were not fitted, because events were few relative to the candidate covariates and several covariates of interest were measured after the time origin. All tests were two-sided with  $\alpha = 0.05$ . No adjustment for multiplicity was made; subgroup analyses are hypothesis-generating.

## Use of a large language model

Claude (Anthropic), a large language model, was used solely as a language-editing aid: to check grammar and improve the English of the author-written text and to correct the formatting of text labels in the figures. It was not used for study design, patient selection, data collection, statistical analysis, interpretation of the data or generation of any result. All suggested edits were reviewed and approved by the authors, who take full responsibility for the content of the manuscript.

## Data availability

The de-identified participant data that support the findings of this study are available from the corresponding author (E.S.) upon reasonable request. The data are not publicly available because they contain information that could compromise the privacy of research participants and are subject to institutional and national restrictions on the sharing of patient-level clinical data.

## Declarations

## Acknowledgements

The authors thank the Turkish Oncology Group and the data managers at each participating center for their assistance with data collection. All figures were prepared by the authors.

## Author contributions

Erdem Sünger: conceptualization, methodology, formal analysis, data curation, investigation, visualization, project administration, writing – original draft, and writing – review and editing. Ahmet Bilici: conceptualization, methodology, supervision, data curation, investigation, and writing – review and editing. Fatih Selçukbiricik and Ömer Fatih Ölmez: data curation, investigation, and writing – review and editing. Bahadır Köylü, Tuğba Akın Telli, Hayati Arvas, Gül Akın, Güneş Dorukhan Çavuşoğlu, Özgür Han, Maral Martin Mildanoğlu, Tuncay Koç, İsmail Bayrakçı, Ergin Aydemir, Nisanur Sarıyar Busery, İlkey Çıtakkul, Ali Kaan Güren, Gülhan İpek Deniz, Abdullah Sakin, Esra Aşık, Safa Can Efil, İrem Uğurlu, Elif Şahin, Murat Araz, Teoman Şakalar, Yakup Ergün, Atike Pınar Erdoğan, Ebru Çiçek, Sakine Damla Açikel Yüksel, Pınar Ezgi Dama, Nargiz Majidova Altuntash, Ayberk Bayramgil, Fatma Keskin Uzundere, Şahin Laçın, İsmail Oğuz Kara, Yasin Kutlu and Erdem Çubukçu: data curation, investigation, and writing – review and editing. All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

## Funding

The authors declare that no funds, grants or other support were received during the preparation of this manuscript.

## Additional information

**Competing interests:** The authors declare no competing interests.

**Correspondence** and requests for materials should be addressed to E.S.

## References

1. Bray, F. et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **74**, 229–263 (2024).
2. Provencio, M. et al. Perioperative nivolumab and chemotherapy in stage III non-small-cell lung cancer. *N Engl. J. Med.* **389**, 504–513 (2023).
3. Caturegli, G. et al. Real-world perioperative outcomes of neoadjuvant chemoimmunotherapy in non-small cell lung cancer. *JTCVS Open.* **28**, 554–564 (2025).
4. NSCLC Meta-analysis Collaborative Group. Preoperative chemotherapy for non-small-cell lung cancer: a systematic review and meta-analysis of individual participant data. *Lancet* **383**, 1561–1571 (2014).
5. Hines, J. B. 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 NSCLC. *J. Thorac. Oncol.* **19**, 1108–1116 (2024).
6. Forde, P. M. et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. *N Engl. J. Med.* **386**, 1973–1985 (2022).
7. Forde, P. M. et al. Overall survival with neoadjuvant nivolumab plus chemotherapy in lung cancer. *N Engl. J. Med.* **393**, 741–752 (2025).
8. Lu, S. et al. Perioperative toripalimab plus chemotherapy for patients with resectable non-small cell lung cancer: the NEOTORCH randomized clinical trial. *JAMA* **331**, 201–211 (2024).
9. Wakelee, H. et al. Perioperative pembrolizumab for early-stage non-small-cell lung cancer. *N Engl. J. Med.* **389**, 491–503 (2023).
10. Spicer, J. D. et al. Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab compared with neoadjuvant chemotherapy alone in patients with early-stage non-small-cell lung cancer (KEYNOTE-671): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* **404**, 1240–1252 (2024).
11. Heymach, J. V. et al. Perioperative durvalumab for resectable non-small-cell lung cancer. *N Engl. J. Med.* **389**, 1672–1684 (2023).
12. Cascone, T. et al. Perioperative nivolumab in resectable lung cancer. *N Engl. J. Med.* **390**, 1756–1769 (2024).
13. Mazieres, J. et al. Immune checkpoint inhibitors for patients with advanced lung cancer and oncogenic driver alterations: results from the IMMUNOTARGET registry. *Ann. Oncol.* **30**, 1321–1328 (2019).
14. Wu, Y. L. et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. *N Engl. J. Med.* **383**, 1711–1723 (2020).

15. Wu, Y. L. et al. Alectinib in resected ALK-positive non-small-cell lung cancer. *N Engl. J. Med.* **390**, 1265–1276 (2024).
16. Cittolin-Santos, G. F. & Rohatgi, A. Neoadjuvant therapy for patients with nonsmall cell lung cancer: not as easy in the real world. *Cancer* **132**, e70312 (2026).
17. Cooper, A. J. et al. Real-world outcomes of neoadjuvant chemoimmunotherapy in patients with nonsmall cell lung cancer: predictors of surgery, pathologic complete response, and event-free survival. *Cancer* **131**, e70081 (2025).
18. Vachtenheim, J. Jr et al. Nationwide implementation of neoadjuvant nivolumab-based chemoimmunotherapy for resectable NSCLC: surgical outcomes from a prospective multicenter study. *Ann. Surg. Oncol.* <https://doi.org/10.1245/s10434-026-20310-2> (2026).
19. Akamine, T. et al. Real-world outcomes of unresected non-small cell lung cancer following neoadjuvant chemoimmunotherapy. *Gen. Thorac. Cardiovasc. Surg.* <https://doi.org/10.1007/s11748-026-02354-z> (2026).
20. Brunelli, A. et al. Surgical results after neoadjuvant nivolumab and platinum-based chemotherapy for resectable lung cancer. A multicentre European real clinical practice analysis. *Eur. J. Cardiothorac. Surg.* **67**, ezaf343 (2025).
21. Shalata, W. et al. Real-world clinical outcomes of neoadjuvant platinum-based chemotherapy with nivolumab in non-small cell lung cancer. *J. Clin. Med.* **13**, 6568 (2024).
22. Qi, Y. et al. Comparison of neoadjuvant chemoimmunotherapy with planned surgery and concurrent chemoradiation followed by immunotherapy for potentially resectable stage III non-small-cell lung cancer: a retrospective study. *Cancer Immunol. Immunother.* **74**, 119. <https://doi.org/10.1007/s00262-025-03961-0> (2025).
23. Faehling, M. et al. Prospective trial of immuno(chemo)therapy before resection, definitive chemoradiotherapy or palliative therapy in patients with locally advanced or oligometastatic non-small cell lung cancer without a primary curative option. *Eur. J. Cancer.* **156**, 175–186 (2021).
24. Adib, E. et al. Definitive radiotherapy with or without chemotherapy after planned neoadjuvant chemoimmunotherapy in stages II to III NSCLC: an international multicenter retrospective study. *JTO Clin. Res. Rep.* **7**, 100949 (2026).
25. Guan, S. et al. Chemoradiotherapy versus surgery after neoadjuvant chemoimmunotherapy in patients with stage III NSCLC: a real-world multicenter retrospective study. *Cancer Immunol. Immunother.* **73**, 120. <https://doi.org/10.1007/s00262-024-03696-4> (2024).
26. Spigel, D. R. et al. Five-year survival outcomes from the PACIFIC trial: durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *J. Clin. Oncol.* **40**, 1301–1311 (2022).
27. Sorin, M. et al. Neoadjuvant chemoimmunotherapy for NSCLC: a systematic review and meta-analysis. *JAMA Oncol.* **10**, 621–633 (2024).
28. Guan, S. et al. Is adjuvant immunotherapy necessary after neoadjuvant chemoimmunotherapy in patients with resectable stage III NSCLC? A two-center real-world study. *Cancer Immunol. Immunother.* **74**, 273. <https://doi.org/10.1007/s00262-025-04130-z> (2025).

29. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human participants. *JAMA* **333**, 71–74 (2025).
30. Eisenhauer, E. A. et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur. J. Cancer*. **45**, 228–247 (2009).
31. Travis, W. D. et al. IASLC multidisciplinary recommendations for pathologic assessment of lung cancer resection specimens after neoadjuvant therapy. *J. Thorac. Oncol.* **15**, 709–740 (2020).
32. Detterbeck, F. C., Boffa, D. J. & Kim, A. W. Tanoue, L. T. The eighth edition lung cancer stage classification. *Chest* **151**, 193–203 (2017).
33. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 (US Department of Health and Human Services, 2017);  
[https://ctep.cancer.gov/protocoldevelopment/electronic\\_applications/ctc.htm](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm)