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Real-world Neoadjuvant Treatment Patterns and Outcomes in Resected Non-Small Cell Lung Cancer

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MICROABSTRACT (60/60)

This study aimed to examine treatment patterns, real-world event-free survival and overall survival among patients with resected, stage II-III NSCLC who received neoadjuvant treatment using SEER-Medicare data (2007-2019). Among 221 patients included, 71% experienced disease recurrence during follow-up; at 5 years, only 20.9% remained event-free and 44.9% stayed alive. These findings highlight the unmet need for more effective neoadjuvant treatments.

ABSTRACT (250/250)

Background: Novel neoadjuvant chemoimmunotherapy treatments are being investigated for locally advanced non-small cell lung cancer (NSCLC), but real-world outcomes for neoadjuvant treatments are poorly understood. This study examined neoadjuvant treatment patterns, real-world event-free survival (rwEFS) and overall survival (OS) in patients with resected, stage II–III NSCLC in the United States (US).

Methods: This retrospective study identified patients in the SEER–Medicare database (2007–2019) with newly diagnosed stage II, IIIA, and IIIB (N2) NSCLC (AJCC 8th edition) treated with neoadjuvant chemo/chemoradiotherapy and resection (index date: neoadjuvant therapy initiation). Neoadjuvant treatment regimens were described. rwEFS (time from index to first recurrence or death, whichever occurred first) and OS (time from index to death) were summarized by Kaplan–Meier analysis for overall population, by disease stage at diagnosis, and by neoadjuvant treatment modality.

Results: 221 patients (stage II, N=70; stage III, N=151) met eligibility criteria. The median follow-up from index was 32.7 months. All patients received neoadjuvant chemotherapy (51%) or chemoradiotherapy (49%) prior to surgery; 97% of patients received platinum-based regimens, among which carboplatin+paclitaxel was the most frequent (45%). In all patients, median rwEFS was 17.6 months and 5-year rwEFS was 20.9%; median OS was 48.5 months and 5-year OS was 44.9%. 71% of patients had disease recurrence during follow-up; among them, 28% developed locoregional recurrence as the first recurrence event.

Conclusions: Patients with resected, stage II–III NSCLC who received neoadjuvant chemo/chemoradiotherapy have high rates of disease recurrence and poor survival outcomes, highlighting need for more effective treatments to improve survival rates.

Keywords: NSCLC, neoadjuvant treatment, real-world event-free survival, overall survival, recurrence

INTRODUCTION

Lung cancer is the most common cause of cancer-related mortality in the United States (US), accounting for 21% of all cancer deaths in 2022.¹ Most cases (85%) are non-small cell lung cancer (NSCLC).^{2,3} The treatment strategy for NSCLC depends on clinical stage and patient performance status.^{4,5} Surgical resection alone is recommended for stage I disease, while multimodality approach is recommended for stage II–III disease.⁶ For certain patients with stage II and N2-negative IIIA NSCLC, neoadjuvant systemic therapy or chemoradiation therapy followed by surgery and adjuvant platinum doublet chemotherapy is a recommended treatment modality, per National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology.⁶ For patients with N2-positive IIIA and select stage IIIB NSCLC, resectability is typically determined by bulk and the extent of nodal involvement. For patients deemed to have resectable disease, neoadjuvant chemotherapy, with or without thoracic radiation, followed by resection has been the standard of care; however, 40%–70% of patients experience disease recurrence after initial treatment.^{7–11} A meta-analysis of randomized controlled trials of patients with stage IB–IIIA disease found that neoadjuvant chemotherapy improved overall survival (OS) and recurrence-free survival rates, with response rates of up to 20%.¹²

Immune checkpoint inhibitors have expanded neoadjuvant treatment options. These agents exploit the anti-programmed death 1 (PD-1) and programmed death ligand 1 (PD-L1) tumor interactions, and have revolutionized treatment of patients with advanced disease and recently demonstrated efficacy and safety in the adjuvant setting.¹³ The PD-1 antibody nivolumab, in combination with platinum-based chemotherapy, is one of the immunotherapies approved by the US Food and Drug Administration (FDA) for neoadjuvant treatment of NSCLC.^{14–16} In addition,

recent results of the CheckMate 77T study have shown that neoadjuvant nivolumab in combination with chemotherapy, followed adjuvant nivolumab, provides statistically significant improvements in event-free survival (EFS) in patients with resectable NSCLC.¹⁷ Recently, based on the significant clinical benefits in patients receiving neoadjuvant pembrolizumab from the KEYNOTE-671 trial,^{18, 19} the FDA approved pembrolizumab with platinum-containing chemotherapy as neoadjuvant treatment for resectable (tumors ≥ 4 cm or node-positive) NSCLC.²⁰ A similar agent, durvalumab, followed by chemotherapy, is also under evaluation in the peri-operative setting in the AEGEAN trial for neoadjuvant treatment of resectable NSCLC.²¹

Given the evolving treatment landscape for resectable NSCLC, an improved understanding of treatment patterns and outcomes of patients in clinical practice can help to define unmet therapeutic needs. In this context, the present study examined the neoadjuvant chemotherapy or chemoradiotherapy regimens, survival outcomes, and recurrence pattern in patients with stage II, IIIA, and IIIB (N2) NSCLC (AJCC 8th edition) in the US.⁷

METHODS

Data source and study design

This retrospective observational study analyzed data from the uniquely-linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database (2007–2019) of patients with newly diagnosed stage II, IIIA, and IIIB (N2) NSCLC (AJCC 8th edition), who received neoadjuvant chemotherapy or chemoradiotherapy and resection. The index date was the date of neoadjuvant treatment initiation, the baseline period was defined as the 12 months preceding the index date, and the study period spanned from the index date to the data cutoff date.

Patient selection

The flow diagram of patient selection is shown in **Figure 1**. Inclusion criteria for patients were as follows: 1) diagnosis of stage II–IIIB (N2) disease (AJCC 8th Edition) NSCLC between 2007 and 2017; 2) age ≥ 66 years at diagnosis; 3) continuous enrollment in Medicare Parts A, B, and D for ≥ 6 months after initial diagnosis⁷; 4) received neoadjuvant chemotherapy or chemoradiotherapy; 5) underwent resection after the initial diagnosis of NSCLC and within 90 days of the end of neoadjuvant therapy; and 6) no diagnoses of distant secondary malignant neoplasm before or within 30 days of surgery. Patients were excluded if they were covered by a health maintenance organization anytime during the study period.

Eligible patients were assigned to recurrence or non-recurrence cohorts based on whether they experienced recurrence during the study period. Recurrence was indicated by a diagnosis of metastatic disease, new diagnosis of locoregional disease, and/or any additional treatments for NSCLC (additional surgery or radiation, chemoradiation, or systemic therapy) following a 90-day interval starting immediately after the initial surgery. The 90-day interval was used to indicate the end of primary treatment and serve as a proxy for disease-free state after surgery.²² There was an extension of the 90-day post-surgery cut off for patients receiving adjuvant chemotherapy and postoperative radiotherapy (PORT). Radiation therapy was considered an adjuvant treatment if initiated within 30 days after completion of adjuvant chemotherapy and within 210 days after the primary surgery.

Study outcomes

Baseline patient characteristics and neoadjuvant treatment patterns, including the proportion of patients receiving chemotherapy or chemoradiation therapy prior to surgery, were described for the overall population and by disease stage.

Survival outcomes included real-world event-free survival (rwEFS), defined as the time from the index date (i.e., start of neoadjuvant therapy) to first disease recurrence or death, whichever occurred first, and OS, defined as the time from the index date to death. For both rwEFS and OS, patients were censored at the earliest of the last date of follow-up in the SEER-Medicare data or end of data availability.

The proportions of patients with locoregional recurrence versus distant metastasis as the first recurrence event were reported.

Statistical analysis

Baseline characteristics were described for all patients and by disease stage. Means and standard deviations were reported for continuous variables, and frequency counts and percentages were reported for categorical variables. rwEFS and OS from the index date were described using Kaplan–Meier (KM) curves for the overall patient population and for patient subgroups stratified by disease stage and by neoadjuvant treatment modality. Neoadjuvant treatment regimens and the proportion of patients on each neoadjuvant treatment regimen were summarized. The proportion of patients with locoregional recurrence versus distant metastasis as the first recurrence event was summarized.

RESULTS

Patient characteristics

A total of 221 patients with resectable NSCLC were included (**TABLES Table 1**). The median follow-up time from initiation of neoadjuvant therapy to death was 32.7 months. At initial diagnosis, 70 patients had stage II disease and 151 had stage III disease. Among patients included, 57% were male and 86% were White.

Neoadjuvant and surgical treatment patterns

Approximately half of patients received neoadjuvant chemotherapy alone (51%) and the remaining received neoadjuvant chemoradiotherapy (49%) (**Table 2**). Most patients (>95%) received platinum-based regimens. Among them, 107 (48.4%) received at least 2 cycles of neoadjuvant chemotherapy treatment and 12 (5.4%) received at least 4 cycles of neoadjuvant chemotherapy treatment. The most frequently used platinum-based regimen was carboplatin + paclitaxel (45%), followed by cisplatin + etoposide (13%), carboplatin + pemetrexed (11%), and cisplatin + pemetrexed (10%). In the overall population, 30% and 25% of patients received adjuvant chemotherapy and PORT, respectively (**Table 2**). In the stage II cohort, 20% received adjuvant chemotherapy and 35% received PORT, respectively. In stage III cohort, 20% received adjuvant chemotherapy and 28% received PORT, respectively.

rwEFS and OS

In the overall patient population, median rwEFS was 17.6 months and 5-year rwEFS was 21% (**Figure 2**). Patients with more advanced disease at initial diagnosis had shorter rwEFS, with a median rwEFS of 16.0 months for stage III disease versus 23.4 months for stage II disease. The 1-, 2-, and 3-year rwEFS following resection were 63%, 49%, and 38%, respectively, for the stage II cohort and 60%, 40%, and 31%, respectively, for the stage III cohort.

For the overall patient population, the median OS was 48.5 months, and 5-year OS was 45% (**Figure 3**). For patients with stage II and III disease, the median OS was 49.4 and 46.9 months, respectively.

rwEFS was comparable between patients who received neoadjuvant chemotherapy and patients who received neoadjuvant chemoradiation therapy (median: 15.3 versus 19.5 months; 5-year rwEFS: 23.5% versus 19.4%) (**Figure 4**). Patients who received neoadjuvant chemotherapy had

numerically higher OS than patients who received neoadjuvant chemoradiation therapy (median OS: 49.6 versus 42.9 months; 5-year OS: 49.9% versus 41.0%) (**Figure 5**).

Recurrence pattern

Out of 221 patients, 156 (71%) had disease recurrence. Among them, 113 (72%) had distant metastasis as the first recurrence event, while 43 (28%) had locoregional recurrence as the first recurrence event.

DISCUSSION

Neoadjuvant chemotherapy can improve post-surgical outcomes for NSCLC, but there is little information on the strategies used and their effectiveness in real-world practice.¹² This study examined neoadjuvant chemotherapy or chemoradiotherapy regimens, recurrence patterns, and survival outcomes (rwEFS and OS) in a cohort of patients with stage II, IIIA, and IIIB (N2) NSCLC in the US. The results showed that nearly all patients received a platinum-based regimen, and almost half received thoracic radiation in the neoadjuvant setting. The median rwEFS was 17.6 months and median OS was 48.5 months for the overall patient population. Over 70% of patients had recurrence during the study period, and most of these patients had distant metastasis as the first recurrence event. These findings provide insight into the use and effectiveness of neoadjuvant chemotherapy and chemoradiotherapy for NSCLC in the US and suggest a need for more effective neoadjuvant treatment options.

Chemotherapy for NSCLC typically consists of a platinum agent paired with gemcitabine, taxanes, or pemetrexed.^{23, 24} The most frequently used neoadjuvant chemotherapy regimen in the present study was carboplatin + paclitaxel, which was also the most common platinum combination in the adjuvant setting in a SEER-Medicare population of patients with stage IB

(tumor size ≥ 4 cm)–IIIB NSCLC,⁸ partners well with concurrent thoracic radiation and is the most widely used regimen in community oncology practices across the US.²⁵ It appears that neoadjuvant therapy followed by resection for locally advanced NSCLC was not widely used in the real world setting, as reflected in **FIGURES**

Figure 1. This less common use of neoadjuvant therapy has also been documented in prior publications. For example, in the large-scale retrospective study of patients with resectable stage III disease, only 2.3% received neoadjuvant treatment followed by surgery as the first-line treatment.²⁶ In addition, a study by Lee et al. 2023 assessing treatment patterns in patients with stage IA–IIIB NSCLC using SEER-Medicare data between 2010 and 2015, found that approximately 8% of patient received neoadjuvant treatment followed by surgery \pm adjuvant treatment.²⁷

The survival results of the present study are consistent with previously published real-world studies. In a multicenter study of patients with stage III (N2) NSCLC who received induction chemotherapy or chemoradiotherapy, the 5-year OS rates ranged between 40% and 43%, and 5-year disease-free survival ranged between 29% and 30%.²⁸ In another large-scale retrospective study of patients with resectable stage III disease treated at 100 centers in 19 countries, the median OS was 49.8 months with preoperative chemotherapy and 44.8 months with preoperative concurrent chemoradiotherapy, while the median PFS was 19.0 and 18.5 months, respectively.²⁶

With the caveat that clinical trial and real-world data are not entirely comparable, our findings are largely aligned with results from previous clinical studies in the neoadjuvant/perioperative setting. For example, a meta-analysis of 15 randomized trials, primarily in patients with stage I–III NSCLC who received neoadjuvant chemotherapy, reported a 5-year OS of 45% and a 5-year recurrence-free survival of 36%.¹² Our study reported a similar 5-year OS rate, but a

lower 5-year EFS rate, which may be driven by how disease recurrence was defined and different patient population in the current study relative to those clinical trials. Additionally, in the phase 3 CheckMate 816 trial that supported the FDA approval of nivolumab plus platinum-doublet chemotherapy as neoadjuvant treatment for resectable NSCLC, the median EFS in patients in the neoadjuvant chemotherapy arm was 20.8 months,¹⁴ which is similar to the median rwEFS of 17.8 months here. It should be noted that in CheckMate 816, 22% of patients in the chemotherapy arm also received optional adjuvant chemotherapy, which is close to the proportion of patients who received (i.e., 30%) adjuvant chemotherapy in the current study. Finally, in the KEYNOTE-671 trial assessing perioperative pembrolizumab in resectable NSCLC,^{18,20} median EFS was 17 months for patients receiving platinum-based neoadjuvant therapy followed by resection. Taken together, the available evidence indicates that there is considerable room for improvement in survival rates with neoadjuvant chemotherapy and chemoradiotherapy options.

Patients who received neoadjuvant chemotherapy had similar rwEFS and numerically higher OS than patients who received neoadjuvant chemoradiation therapy. While the study was not designed to compare these two neoadjuvant treatment modalities in patients with NSCLC, and the analyses are descriptive in nature, the findings are largely aligned with existing literature, as no consistent evidence showing survival benefits from neoadjuvant chemotherapy versus neoadjuvant chemoradiation therapy has been presented.^{29,30}

Treatment of NSCLC at an early stage can alter the disease course and prolong survival.³¹ It has been suggested that immunotherapy can be especially beneficial in the neoadjuvant setting because the range of neoantigens present on intact tumors can stimulate T cell activation, leading to eradication of micrometastases.³² Additionally, tumor antigens released as a consequence of chemotherapy-induced tumor cell death potentiate the immune response; thus, chemotherapy in

combination with immunotherapy may exert a synergistic antitumor effect. Numerous ongoing trials, including CheckMate 77T (nivolumab),³³ Impower 030 (atezolizumab),³⁴ and Aegean (durvalumab)³⁵ are investigating the efficacy of perioperative immunotherapy–chemotherapy combinations for stages II–IIIB NSCLC, suggesting a potential shift from neoadjuvant to perioperative systemic therapies in this population. In KEYNOTE-671, a regimen of neoadjuvant pembrolizumab plus chemotherapy and adjuvant pembrolizumab monotherapy was associated with a significant improvement in EFS and OS, as well as higher rates of pathologic complete response and major pathologic response compared with a placebo plus chemotherapy combination.^{18, 19, 36, 37} EFS benefits were also observed in patients receiving neoadjuvant nivolumab plus chemotherapy, followed by adjuvant nivolumab, in the CheckMate 77T trial, and in patients receiving neoadjuvant durvalumab plus chemotherapy, followed by adjuvant durvalumab in the Aegean trial.^{17, 21}

This study had certain limitations. First, the linked SEER–Medicare database only includes patients with Medicare insurance (i.e., ≥ 65 years old); therefore, the results from this study may not reflect outcomes in a younger patient population. However, in the US, over 70% of patients with lung cancer between 2015–2019 were diagnosed at the age of 65 or above, with the median age at diagnosis being 71 years.³⁸ Second, as the data used in this study were from 2007 to 2019 (before the approval of neoadjuvant immunotherapy for NSCLC in the US), the analyses are limited to patients who received neoadjuvant chemotherapy and chemoradiotherapy. Third, because of the nature of administrative claims data, NSCLC recurrence could not be identified directly; therefore, the algorithm used relied on various procedure, diagnosis, and drug codes and employed certain assumptions. Coding inaccuracies may have led to misclassification bias and misidentification of patients with NSCLC recurrence. Patients who did not receive treatment in

the event of recurrence or did not have codes associated with metastasis in their claims were also missed. Fourth, some clinical information, such as surgical outcomes (i.e., complete or incomplete resection status), were not available in the data. Therefore, a 90-day interval was used to indicate the end of primary treatment and serve as a proxy for disease-free state. Fifth, while the database used in this study was uniquely able to provide long-term outcomes on SEER patients, the requirement to be a Medicare beneficiary throughout the entire length of the study excluded many from the SEER population, resulting in a relatively small sample size. Additional real-world studies with a larger sample can provide greater insight into the treatment patterns and outcomes of patients with resectable NSCLC. Finally, SEER data lack some lung-cancer specific granularity and does not include information on treatment facility type, methods for nodal staging, number of chemotherapy cycles, or pathologic response to induction treatment. Future studies using a database with this information may be warranted.

CONCLUSION

The results of this real-world study of patients with stages II, IIIA, and IIIB (N2) NSCLC in the US show that despite receiving neoadjuvant chemotherapy or chemoradiotherapy, the majority of patients experienced disease recurrence within 2 years of initial treatment. The median rwEFS was only 18 months, and OS was 49 months for the overall population. These findings highlight a need for more effective treatments for NSCLC at a resectable stage of disease in order to prevent recurrence and improve survival rates.

CLINICAL PRACTICE POINTS (198/250 words)

Multimodality treatment, including neoadjuvant chemotherapy with or without thoracic radiation, followed by surgery, is conventionally recommended for patients with resectable, stage II–III NSCLC. However, 40% to 70% of patients with resected NSCLC tumors experience recurrence after initial treatment. An evaluation of historical real-world treatment patterns and outcomes of patients with stage II–III resected NSCLC, who received neoadjuvant chemotherapy or chemoradiation therapy, will help to better understand the unmet needs of this population. This observational retrospective study used data from the SEER-Medicare database (2007–2019) and found that, among 221 patients with newly diagnosed stage II–IIIB (N2; AJCC 8th edition) NSCLC who received neoadjuvant chemotherapy or chemoradiotherapy and resection, 71% had disease recurrence during the course of follow-up (median 32.7 months). The median rwEFS and OS was 17.6 months years and 48.5 months, respectively, and the 5-year rwEFS and OS rates were 20.9% and 44.9%, respectively. Approximately 30% patients with disease recurrence had loco-regional recurrence as the first recurrence. As novel neoadjuvant treatments for NSCLC, such as immunotherapy and targeted therapy are emerging, the suboptimal treatment patterns and outcomes observed highlight the importance of more effective treatment options for patients with stage II–III resected NSCLC to improve survival outcomes.

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Author contributions

Su Zhang, Yan Song, Chi Gao, Ari Lerner, Anya Jiang, and James Signorovitch contributed to study conception and design, data collection and assembly, and data analysis and interpretation. Jessica Donington, Ashwini Arunachalam, Diana Chirovsky, Ayman Samkari, and Xiaohan Hu contributed to study conception and design and data analysis and interpretation. All authors reviewed and approved the final content of this manuscript.

Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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Data statement

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

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Ethics statement

The data used in this study were limited and complied with the Health Insurance Portability and Accountability Act and the Declaration of Helsinki.

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TABLES

Table 1. Baseline characteristics of patients with NSCLC by disease stage

	Overall (N = 221)	Stage II disease (N = 70)	Stage III disease (N = 151)
Demographic characteristics			

Age at surgery, years	72.1 ± 4.9	72.2 ± 4.8	72.1 ± 4.9
Male	126 (57%)	37 (52.9%)	89 (58.9%)
Race/ethnicity			
White	191 (86.4%)	59 (84.3%)	132 (87.4%)
Non-White	30 (13.6%)	11 (15.7%)	19 (12.6%)
Year of surgery			
2007–2009	51 (23.1%)	19 (27.1%)	32 (21.2%)
2010–2012	63 (28.5%)	19 (27.1%)	44 (29.1%)
2013–2014	44 (19.9%)	15 (21.4%)	29 (19.2%)
2015–2018	63 (28.5%)	17 (24.3%)	46 (30.5%)
Clinical characteristics			
CCI	1.4 ± 1.4	1.7 ± 1.4	1.2 ± 1.3
Histology type			
Squamous	89 (40.3%)	34 (48.6%)	55 (36.4%)
Non-squamous/NOS	132 (59.7%)	36 (51.4%)	96 (63.6%)

Data are presented as mean \pm standard deviation or n (%).

Non-White racial/ethnic groups included patients with Black, Hispanic, Asian and Other ethnicity. The specific number of patients in these racial/ethnic groups were <11 and thus were not reported due to the minimum cell size requirement by SEER-Medicare.

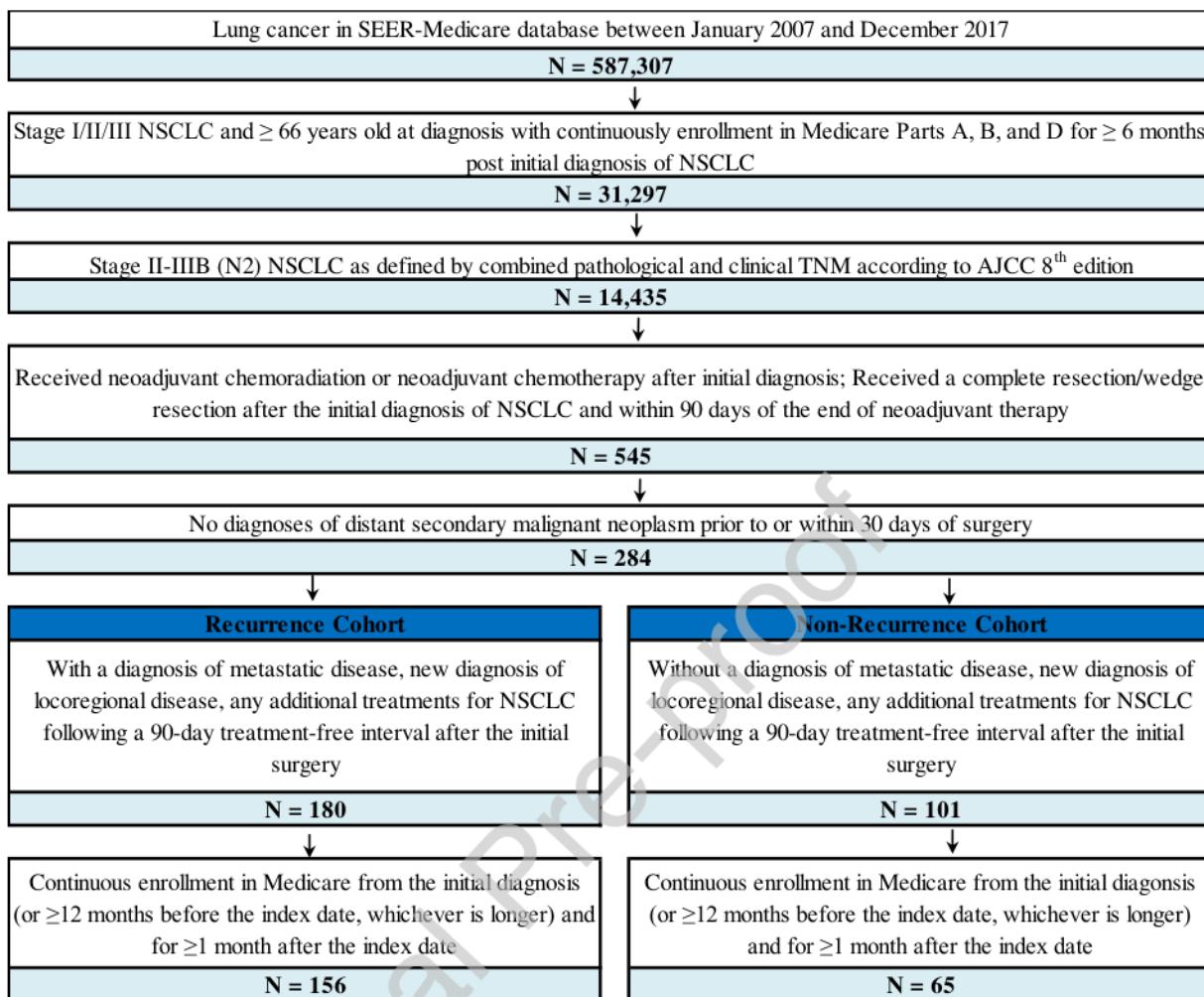
Abbreviations: CCI, Charlson Comorbidity Index; NOS, not otherwise specified; NSCLC, non-small cell lung cancer.

Table 2. Neoadjuvant treatment patterns and primary surgical treatment patterns

	Number (%) of patients
Neoadjuvant treatment	
With neoadjuvant radiotherapy	108 (49%)
Platinum-based therapy	>210 (>95%)
Carboplatin + paclitaxel	100 (45.2%)
Cisplatin + etoposide	28 (12.7%)
Carboplatin + pemetrexed	25 (11.3%)
Cisplatin + pemetrexed	21 (9.5%)
Non-platinum-based therapy	<11 (<5%)
Primary surgical treatment	
Type of surgery	
Lobectomy	197 (89.1%)
Adjuvant chemotherapy, N (%)	67 (30.3%)
Postoperative radiotherapy, N (%)	56 (25.3%)

FIGURES

Figure 1. Sample selection and creation of patient cohorts



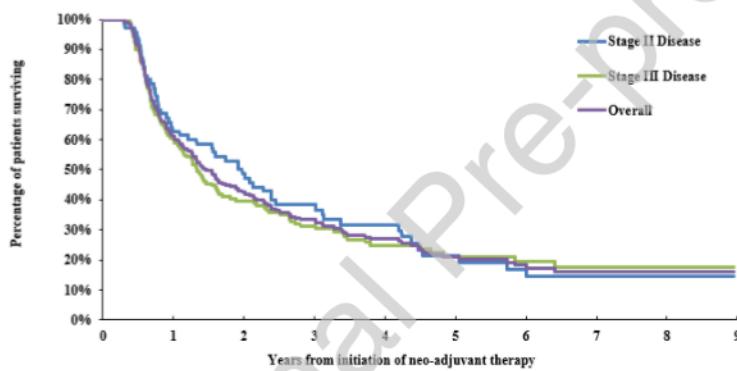
Abbreviations: AJCC, American Joint Committee on Cancer; NSCLC, non-small cell lung cancer; SEER, Surveillance, Epidemiology, and End Results; TNM, tumor node metastasis.

Note:

The following International Classification of Diseases for Oncology, Third Edition, codes were considered to identify patients with NSCLC: C340-C343, C348, and C349 with the relevant histology codes (8010, 8012, 8013, 8020, 8046, 8050–8052, 8070–8078, 8140, 8141, 8143, 8147, 8250–8255, 8260, 8310, 8430, 8480, 8481, 8490, 8560, and 8570–8575.

Figure 2. Kaplan–Meier analysis of real-world event-free survival in patients with non-small cell lung cancer treated with neoadjuvant therapy stratified by disease stage

Cohorts	Total number of patients	Real-world event-free survival rate								Censored	Median survival (months)
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year		
Stage II Disease	70	62.9%	48.6%	38.4%	31.6%	21.3%	17.0%	14.6%	14.6%	15	23.38
Stage III Disease	151	60.3%	39.6%	31.1%	24.8%	21.1%	19.4%	17.5%	17.5%	36	15.98
Overall	221	61.1%	42.4%	33.3%	26.9%	20.9%	18.3%	16.2%	16.2%	51	17.59

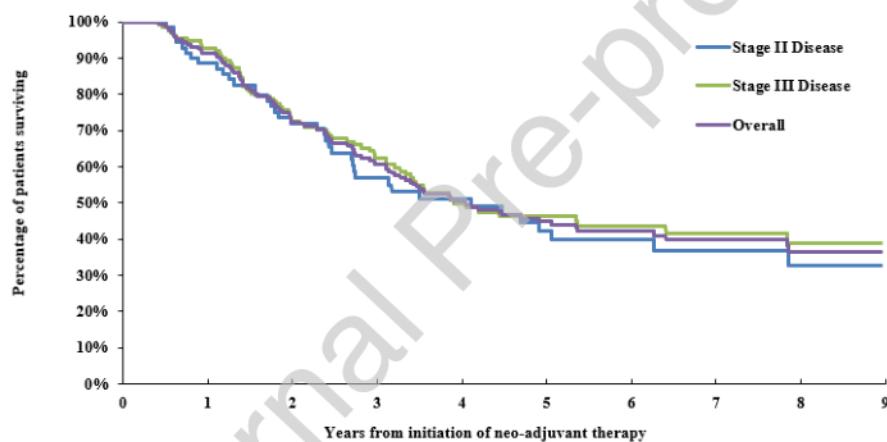


Years from initiation	0	1	2	3	4	5	7	9
Patients at risk	70	44	34	23	n*	n*	n*	n*
Stage II	70	44	34	23	n*	n*	n*	n*
Stage III	151	90	52	38	16	n*	n*	n*
Overall	221	134	86	61	26	13	n*	n*

n* represents sample size <11.

Figure 3. Kaplan–Meier analysis of overall survival in patients with non-small cell lung cancer treated with neoadjuvant therapy stratified by disease stage

Cohorts	Total number of patients	Overall survival rate								Censored	Median survival (months)
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year		
Stage II Disease	70	88.5%	72.0%	56.8%	51.1%	42.2%	39.7%	36.7%	32.6%	32	49.35
Stage III Disease	151	92.7%	72.6%	62.5%	49.7%	46.4%	43.6%	41.5%	38.9%	78	46.85
Overall	221	91.4%	72.4%	60.6%	50.3%	44.9%	42.2%	39.7%	36.6%	110	48.53



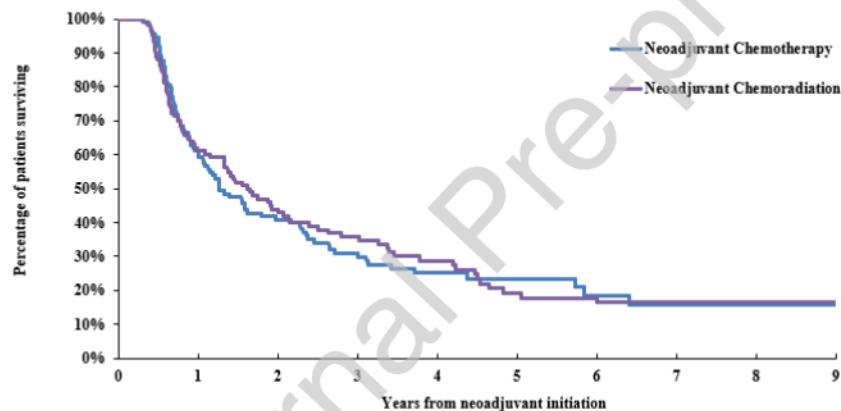
Years from initiation	0	1	2	3	5	7	9
Patients at risk	70	60	47	31	17	n*	n*
Stage II	70	60	47	31	17	n*	n*
Stage III	151	136	92	70	35	19	n*
Overall	221	196	139	101	52	30	n*

n* represents sample size <11.



Figure 4. Kaplan–Meier analysis of real-world event-free survival in patients with non-small cell lung cancer treated with neoadjuvant therapy stratified by neoadjuvant treatment modality

Cohorts	Total number of patients	Real-world recurrence-free survival rate								Censored	Median survival (months)
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year		
Neoadjuvant Chemotherapy	113	61.1%	40.9%	31.0%	25.2%	23.5%	18.5%	15.9%	15.9%	28	15.31
Neoadjuvant Chemoradiation	108	61.1%	44.0%	35.8%	28.8%	19.2%	17.9%	16.4%	16.4%	23	19.47

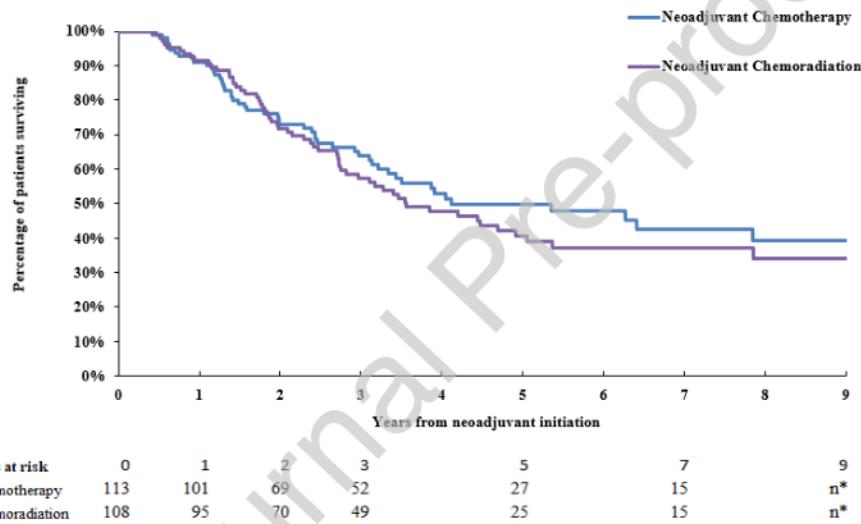


Years from initiation	0	1	2	3	5	7	9
Patients at risk	113	68	42	29	12	n*	n*
Chemotherapy	113	68	42	29	12	n*	n*
Chemoradiation	108	66	44	32	14	n*	n*

n* represents sample size <11.

Figure 5. Kaplan–Meier analysis of overall survival in patients with non-small cell lung cancer treated with neoadjuvant therapy stratified by neoadjuvant treatment modality

Cohorts	Total number of patients	Real-world overall survival rate								Censored	Median survival (months)
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year		
Neoadjuvant Chemotherapy	113	91.1%	73.1%	64.0%	53.0%	49.9%	48.0%	42.6%	39.4%	62	49.62
Neoadjuvant Chemoradiation	108	91.6%	71.8%	57.3%	47.7%	40.6%	37.1%	37.1%	34.0%	48	42.91



n* represents sample size <11.