Original Study

Treatment Patterns and Health Resource Utilization Among Patients Diagnosed With Early Stage Resected Non–Small Cell Lung Cancer at US Community Oncology Practices

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Abstract

Data on adjuvant therapy in resected non–small cell lung cancer (NSCLC) in routine practice are lacking in the United States. This retrospective observational database study included 609 community oncology patients with resected stage IB to IIIA NSCLC. Use of adjuvant therapy was 39.1% at disease stage IB and 64.9% to 68.2% at stage II to IIIA. The most common regimen at all stages was carboplatin and paclitaxel.

Background: Platin-based adjuvant chemotherapy has extended survival in clinical trials in patients with completely resected non–small cell lung cancer (NSCLC). There are few data on the use of adjuvant therapy in community-based clinical practice in the United States. **Materials and Methods:** This was a retrospective observational study using electronic medical record and billing data collected during routine care at US community oncology sites in the Vector Oncology Data Warehouse between January 2007 and January 2014. Patients aged ≥ 18 years with a primary diagnosis of stage IB to IIIA NSCLC were eligible if they had undergone surgical resection. Treatment patterns, health care resource use, and cost were recorded, stratified by stage at diagnosis. **Results:** The study included 609 patients (mean age, 64.8 years, 52.9% male), of whom 215 had stage IB disease, 130 stage IIA/II, 110 stage IIB, and 154 stage IIIA. Adjuvant systemic therapy after resection was provided to 345 (56.7%) of 609 patients, with lower use in patients with stage IB disease (39.1%) than stage II to IIIA disease (64.9-68.2%) ($P < .0001$). The most common adjuvant regimen at all stages was the combination of carboplatin and paclitaxel. There were no statistically significant differences in office visits or incidence of hospitalization by disease stage. During adjuvant treatment, the total monthly median cost per patient was $17,389.75 (interquartile range, $8,815.61 to $23,360.85). **Conclusion:** Adjuvant systemic therapy was used in some patients with stage IB NSCLC and in the majority of patients with stage IIA to IIIA disease. There were few differences in regimen or health care resource use by disease stage.

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Introduction

Lung cancer is the leading cause of cancer deaths in the United States (US), with an estimated 159,480 deaths in 2013.[1] Approximately 84% of lung cancers are classified as non–small cell lung cancer (NSCLC).[1] The 5-year survival rate across all stages of NSCLC has been estimated at 16%, increasing to 52% for the 15% of cases diagnosed at a localized stage.[1] Complete surgical resection is the standard treatment for localized NSCLC.[2] Despite complete resection, the disease recurs in a high proportion of patients.[2,3] Adjuvant chemotherapy can help to reduce the risk of recurrence after surgery and has been investigated in several clinical trials.[4-8] Survival benefits have been demonstrated for patients with completely resected NSCLC receiving adjuvant chemotherapy with cisplatin-based regimens,[4] cisplatin plus vinorelbine,[5,6] and carboplatin plus paclitaxel in patients with resected stage IB NSCLC with

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tumors ≥ 4 cm in diameter.[7] Platin-based adjuvant chemotherapy is now considered the standard of care in completely resected NSCLC for patients with good performance status.[2]

Few studies have investigated the extent to which these clinical trial findings have been taken up in routine community-based clinical practice, and data on treatment patterns are lacking for the US.

The purpose of the present study was to describe recent treatment patterns and health resource utilization (including cost) for patients with stage IB to IIIA NSCLC treated in community oncology practices in the US, who have undergone surgical resection of their disease. The primary objective was to describe patterns of systemic treatment (excluding neoadjuvant therapy) by disease stage at diagnosis. Secondary objectives included describing the clinical characteristics of patients by stage, disease-free survival, treatment patterns by starting date of adjuvant treatment from diagnosis (early compared to late), and health care resource utilization and cost by disease stage.

Materials and Methods

Study Design

This was a retrospective observational study (GSK study identifier: HO-13-13748) of treatment patterns, using data collected between January 2007 and January 2014 as part of routine care for adult patients with a primary diagnosis of NSCLC in community oncology settings in the US. Data were obtained from the Vector Oncology Data Warehouse, which contains electronic medical records and billing data collected at a network of community oncology practices mainly in the Southern and Midwestern US.

Study Endpoints

The primary endpoint was treatment pattern by stage at initial diagnosis. Other endpoints included demographic and clinical characteristics, disease-free survival, and health care resource use and cost, stratified by disease stage at diagnosis.

Patient Population

All potentially eligible patients in the database were screened for inclusion, and patients who met the eligibility criteria were accrued in random order until the target number of 600 patients was met. Patients were drawn from the Vector Oncology Data Warehouse, and the study sample consisted of those diagnosed with NSCLC between January 1, 2007, and September 1, 2013.

Eligible patients met the following criteria: confirmed diagnosis of lung cancer, indicated by a statement in the medical record and an International Classification of Diseases Ninth Revision (ICD-9) diagnostic code of 162.2 to 162.9; confirmed non−small cell disease type; aged at least 18 years at time of diagnosis; and staged clinically or pathologically at stage IB to IIIA. In addition, for inclusion, patients had to have undergone a qualifying surgical resection, defined as any surgical resection other than a wedge resection or segmentectomy for curative treatment of NSCLC as of the date of data collection. Patients who underwent a qualifying surgical resection within 30 days after a wedge resection or segmentectomy qualified for inclusion.

Patients with stage IA disease, or with disease first diagnosed at stage IIIB or IV, were excluded from the study.

Data Collection

Patients were initially identified by Structured Query Language (SQL) database queries, and eligibility was confirmed through review of medical records by a clinical research nurse. Data were extracted partly by SQL queries and partly by visual review of records by clinical research nurses.

The extracted data included: date of birth; date of death; date of last office visit for patients with no recurrence; ethnicity and gender; date of initial NSCLC diagnosis; date and type of resection; whether the patient received radiotherapy and/or neoadjuvant therapy (with the start and end date of radiotherapy if used, and whether radiotherapy was concurrent with systemic therapy); disease stage (initial stage if sequential progressive stages were recorded, and pathologic stage preferred to clinical stage if both were available); details of any oral, subcutaneous, or intravenous chemotherapy, targeted therapy, or hormone therapy after resection up to and including the first systemic therapy after disease recurrence or the end of the medical record, whichever occurred first; date and type (local, regional, or distant) of first disease recurrence after resection; biomarker tests for epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (*ALK*), melanoma-associated antigen 3 (*MAGE-A3*), Kirsten rat sarcoma viral oncogene (*KRAS*), or receptor tyrosine kinase (*ROS1*); and billing record data.

The extracted data were used to derive the patient's age at diagnosis, treatment regimens used, cost of treatment (directly obtained from the database for injectable therapies, estimated from unit costs and duration of therapy for oral agents), and duration of therapy. A treatment regimen was defined as 1 or more anticancer agents provided over a period of time, provided that all agents started within 30 days of the start of the first agent and that no agent was discontinued and replaced within 30 days of the start of the first agent. Adjuvant therapy was defined as the first systemic therapy delivered after diagnosis and resection. Therapy after disease recurrence was defined as the first systemic therapy delivered after the first disease recurrence.

The study sample was divided into 3 cohorts on the basis of the timing of their adjuvant treatment start date relative to their date of diagnosis: early, late, and no adjuvant therapy administered. The median time between date of diagnosis and date of start of therapy for those who were administered adjuvant therapy was used to divide patients into early versus late treatment initiation.

Data Analysis

Study variables were analyzed using descriptive statistics (eg, mean, standard deviation [SD], standard error [SE], frequency, and percentage). The Kaplan-Meier product limit estimator was used to describe time-to-event outcomes (eg, duration of therapy and disease-free survival). For time-to-event analyses that included patients who did not receive systemic therapy, the time origin was the date of resection. For analyses that included only patients who received systemic therapy, the time origin was the start of systemic therapy after diagnosis and resection.

Cost of care included only services delivered through the oncology practice, including systemic therapy, other drugs, office visits, and other procedures. Costs (except the cost for oral therapies) were taken from the amount charged by the oncology practice as indicated by the billing system records, inflated to 2013 US$

Table 1 Demographic and Clinical Characteristics of Patients by Disease Stage

Parameter	Disease Stage					*P*
	IB (n = 215)	IIA/II (n = 130)	IIB (n = 110)	IIIA (n = 154)	Overall (n = 609)	
Mean (SD) age at diagnosis, years[a]	65.81 (10.33)	64.22 (9.84)	64.13 (9.69)	64.15 (9.44)	64.75 (9.90)	.3005[c]
No. of subjects with date of diagnosis available	207	123	103	149	582	
Gender, n (%)						.4054[d]
Male	108 (50.2%)	65 (50.0%)	65 (59.1%)	84 (54.5%)	322 (52.9%)	
Female	107 (49.8%)	65 (50.0%)	45 (40.9%)	70 (45.5%)	287 (47.1%)	
Race, n (%)						.6274[e]
White	128 (59.5%)	71 (54.6%)	60 (54.5%)	99 (64.3%)	358 (58.8%)	
Black	20 (9.3%)	11 (8.5%)	13 (11.8%)	17 (11.0%)	61 (10.0%)	
Asian	2 (0.9%)	1 (0.8%)	1 (0.9%)	2 (1.3%)	6 (1.0%)	
Hispanic	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.6%)	2 (0.3%)	
Other	2 (0.9%)	2 (1.5%)	1 (0.9%)	0 (0.0%)	5 (0.8%)	
Not documented	63 (29.3%)	45 (34.6%)	34 (30.9%)	35 (22.7%)	177 (29.1%)	
Region of Patient Residence, n (%)						.4639[f]
Northeast	3 (1.4%)	1 (0.8%)	2 (1.8%)	0 (0.0%)	6 (1.0%)	
South	179 (83.3%)	111 (85.4%)	96 (87.3%)	126 (81.8%)	512 (84.1%)	
Midwest	33 (15.3%)	18 (13.8%)	12 (10.9%)	28 (18.2%)	91 (14.9%)	
Type of Surgical Resection, n (%)						.0046[e]
Bilobectomy	9 (4.2%)	5 (3.8%)	3 (2.7%)	10 (6.5%)	27 (4.4%)	
Lobectomy	192 (89.3%)	111 (85.4%)	91 (82.7%)	118 (76.6%)	512 (84.1%)	
Pneumonectomy	8 (3.7%)	8 (6.2%)	15 (13.6%)	22 (14.3%)	53 (8.7%)	
Sleeve lobectomy	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	
Not specified	6 (2.8%)	4 (3.1%)	1 (0.9%)	4 (2.6%)	15 (2.5%)	
Radiotherapy, n (%)						<.0001[d]
Yes	27 (12.6%)	22 (16.9%)	24 (21.8%)	54 (35.1%)	127 (20.9%)	
No	179 (83.3%)	103 (79.2%)	84 (76.4%)	96 (62.3%)	462 (75.9%)	
Unknown	9 (4.2%)	5 (3.8%)	2 (1.8%)	4 (2.6%)	20 (3.3%)	
Neoadjuvant Therapy, n (%)						<.0001[f]
Yes	6 (2.8%)	7 (5.4%)	13 (11.8%)	38 (24.7%)	64 (10.5%)	
No	206 (95.8%)	123 (94.6%)	96 (87.3%)	115 (74.7%)	540 (88.7%)	
Unknown	3 (1.4%)	0 (0.0%)	1 (0.9%)	1 (0.6%)	5 (0.8%)	
EGFR Testing, n (%)						.0897[d]
Tested	30 (14.0%)	16 (12.3%)	13 (11.8%)	35 (22.7%)	94 (15.4%)	
Positive[b]	9 (30.0%)	3 (18.8%)	4 (30.8%)	1 (2.9%)	17 (18.1%)	.0075[f]
Negative[b]	21 (70.0%)	13 (81.3%)	9 (69.2%)	34 (97.1%)	77 (81.9%)	
Not tested	47 (21.9%)	23 (17.7%)	18 (16.4%)	28 (18.2%)	116 (19.0%)	
Unknown	138 (64.2%)	91 (70.0%)	79 (71.8%)	91 (59.1%)	399 (65.5%)	

Abbreviations: EGFR = epidermal growth factor receptor; SD = standard deviation.
[a]Mean age at diagnosis could not be calculated for some patients due to incomplete data on the date of diagnosis.
[b]Percentage of patients tested.
[c]ANOVA, under assumption of equal group variances.
[d]Chi-square test.
[e]Monte Carlo exact test.
[f]Fisher exact test.

based on the consumer price index for pharmaceuticals and physician services. Costs for oral therapies were calculated from the drug name, dose, and start/stop dates in the records, using average wholesale prices. Costs incurred outside the oncology practice, such as hospital costs, were not included. Cost and health care resource use were estimated for 2 time periods: the duration of adjuvant therapy, and the time from diagnosis to the end of the initial regimen after disease recurrence or the end of the medical record, whichever occurred first. To adjust for variable follow-up times across patients, median monthly costs per patient were calculated on the basis of the months of follow-up of interest and the costs accumulated over the period of interest.

Table 2 Systematic Therapy Treatment Patterns by Disease Stage

Regimen	Disease Stage				Overall (n = 609)
	IB (n = 215)	IIA/II (n = 130)	IIB (n = 110)	IIIA (n = 154)	
Adjuvant Therapy After Resection, n (%)					
Patients receiving adjuvant therapy	84 (39.1%)	86 (66.2%)	75 (68.2%)	100 (64.9%)	345 (56.7%)
Patients receiving second adjuvant therapy	6 (2.8%)	12 (9.2%)	12 (10.9%)	12 (7.8%)	42 (6.9%)
Patients receiving third adjuvant therapy	3 (1.4%)	1 (0.8%)	1 (0.9%)	0 (0.0%)	5 (0.8%)
Adjuvant Therapy, Most Common[a] First Regimen, n (%)[b]					
Carboplatin	5 (6.0%)	5 (5.8%)	2 (2.7%)	11 (11.0%)	23 (6.7%)
Carboplatin, paclitaxel	25 (29.8%)	21 (24.4%)	23 (30.7%)	34 (34.0%)	103 (29.9%)
Carboplatin, pemetrexed	8 (9.5%)	2 (2.3%)	3 (4.0%)	5 (5.0%)	18 (5.2%)
Cisplatin	9 (10.7%)	15 (17.4%)	9 (12.0%)	15 (15.0%)	48 (13.9%)
Cisplatin, docetaxel	9 (10.7%)	12 (14.0%)	9 (12.0%)	9 (9.0%)	39 (11.3%)
Cisplatin, pemetrexed	7 (8.3%)	9 (10.5%)	5 (6.7%)	4 (4.0%)	25 (7.2%)
Cisplatin, vinorelbine	6 (7.1%)	5 (5.8%)	6 (8.0%)	11 (11.0%)	28 (8.1%)
Other	15 (17.9%)	17 (19.8%)	18 (24.0%)	11 (11.0%)	61 (17.7%)
Adjuvant Therapy, Most Common[a] Second Regimen, n (%)[c]					
Carboplatin	0 (0.0%)	2 (16.7%)	3 (25.0%)	3 (25.0%)	8 (19.0%)
Carboplatin, docetaxel	0 (0.0%)	3 (25.0%)	1 (8.3%)	0 (0.0%)	4 (9.5%)
Carboplatin, paclitaxel	1 (16.7%)	3 (25.0%)	2 (16.7%)	5 (41.7%)	11 (26.2%)
Carboplatin, pemetrexed	1 (16.7%)	2 (16.7%)	1 (8.3%)	1 (8.3%)	5 (11.9%)
Other	4 (66.7%)	2 (16.7%)	5 (41.7%)	3 (25.0%)	14 (33.3%)
Therapy After Disease Recurrence, n					
Patients receiving therapy after disease recurrence	17	15	13	23	68
Therapy After Disease Recurrence, Most Common[a] Regimen, n (%)[d]					
Bevacizumab, carboplatin, paclitaxel	2 (11.8%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	4 (5.9%)
Carboplatin	1 (5.9%)	0 (0.0%)	1 (7.7%)	4 (17.4%)	6 (8.8%)
Carboplatin, paclitaxel	4 (23.5%)	4 (26.7%)	3 (23.1%)	6 (26.1%)	17 (25.0%)
Carboplatin, pemetrexed	1 (5.9%)	0 (0.0%)	0 (0.0%)	3 (13.0%)	4 (5.9%)
Cisplatin	2 (11.8%)	2 (13.3%)	0 (0.0%)	1 (4.3%)	5 (7.4%)
Erlotinib	3 (17.6%)	1 (6.7%)	1 (7.7%)	2 (8.7%)	7 (10.3%)
Pemetrexed	1 (5.9%)	2 (13.3%)	3 (23.1%)	1 (4.3%)	7 (10.3%)
Other	3 (17.6%)	4 (26.7%)	5 (38.5%)	6 (26.1%)	18 (26.5%)

[a]Received by > 5% of patients overall.
[b]Percentage of patients receiving adjuvant therapy.
[c]Percentage of patients receiving second adjuvant therapy regimen.
[d]Percentage of patients receiving therapy after disease recurrence.

For analyses in which 3 or more groups were compared, *P* values were from analysis of variance (ANOVA) or a nonparametric Kruskal-Wallis test for continuous variables and a chi-square test or the Fisher exact test for categorical variables. In instances where exact computations would have required a large amount of time and memory, *P* values were estimated by Monte Carlo estimation. We used *SAS* software (SAS Institute, Cary, NC) to perform Monte Carlo estimation by specifying the MC computation option in the EXACT statement of the frequency procedure. Direct statistical comparisons of cost were not conducted.

Results

Demographic and Clinical Characteristics

A total of 609 patients met all the eligibility criteria and were included in the final analysis. Table 1 shows the demographic and clinical characteristics of the patients, overall and by disease stage at diagnosis. There were no statistically significant differences in demographics (age, gender, race, region) across the disease stages. Lobectomy was the most common resection procedure at all disease stages, although patients with the highest disease stage (stage IIIA) were less likely to have undergone lobectomy compared to patients with disease at earlier stages ($P = .0035$). The proportion of patients who received radiotherapy increased with higher disease stage. Most patients did not receive neoadjuvant therapy, although it was more commonly provided to patients with higher disease stage. The only biomarker tested in more than 10% of patients overall was EGFR, which was tested for in 15.4% of patients. Overall, 81.9% of patients tested were EGFR negative.

Table 3 Health Care Resource Use During Adjuvant Therapy as Well as From Diagnosis to End of First Regimen After Disease Recurrence or End of Medical Record by Disease Stage

Parameter	Disease Stage					
During Adjuvant Therapy	**IB (n = 63)**	**IIA/II (n = 52)**	**IIB (n = 48)**	**IIIA (n = 65)**	**Overall (n = 228)**	***P***
Office Visits						
Incidence, n (%)	62 (98.4%)	52 (100.0%)	48 (100.0%)	65 (100.0%)	227 (99.6%)	.7149[a]
Frequency, mean (SD)	11.25 (7.64)	9.15 (4.24)	12.40 (7.71)	12.40 (11.30)	11.34 (8.36)	.1461[b]
Hospitalizations						
Incidence, n (%)	12 (19.0%)	3 (5.8%)	7 (14.6%)	13 (20.0%)	35 (15.4%)	.1423[c]
Frequency, mean (SD)	0.38 (0.87)	0.06 (0.24)	0.23 (0.63)	0.31 (0.68)	0.25 (0.67)	.0308[d]
Duration (days), mean (SD)	5.75 (4.56)	3.67 (2.08)	5.57 (4.54)	7.46 (8.82)	6.17 (6.28)	.8862[e]
From Diagnosis to End of First Regimen after Disease Recurrence or End of Medical Record	**IB (n = 158)**	**IIA/II (n = 81)**	**IIB (n = 67)**	**IIIA (n = 101)**	**Overall (n = 407)**	***P***
Office Visits						
Incidence, n (%)	151 (95.6%)	77 (95.1%)	64 (95.5%)	92 (91.1%)	384 (94.3%)	.4875[a]
Frequency, mean (SD)	13.29 (15.19)	12.86 (8.91)	17.39 (12.30)	16.54 (15.90)	14.69 (13.97)	.0639[b]
Hospitalizations						
Incidence, n (%)	63 (39.9%)	21 (25.9%)	31 (46.3%)	39 (38.6%)	154 (37.8%)	.0653[c]
Frequency, mean (SD)	0.72 (1.08)	0.30 (0.56)	0.73 (0.96)	0.67 (1.03)	0.63 (0.97)	.0025[d]
Duration (days), mean (SD)	6.13 (5.54)	3.38 (2.36)	6.06 (4.71)	7.72 (8.02)	6.14 (5.93)	.1280[e]

Abbreviation: SD = standard deviation.
[a]Fisher exact test.
[b]ANOVA, under assumption of equal group variances.
[c]Chi-square test.
[d]Negative binomial regression.
[e]Kruskal-Wallis test.

Treatment Patterns

Table 2 shows the numbers of patients who received adjuvant chemotherapy and the most commonly used systematic treatment regimens (defined as those used in > 5% of patients who received adjuvant therapy). Adjuvant therapy after resection was administered to 345 (56.7%) of 609 patients overall. The proportion of patients receiving adjuvant therapy was lower in patients with the earliest stage of disease at diagnosis, stage IB (39.1%), compared to patients at a relatively more advanced stage II to IIIA disease (64.9-68.2%) ($P < .0001$).

The most commonly used adjuvant therapy regimen was a combination of carboplatin and paclitaxel, used in 103 (29.9%) of 345 patients. Of the patients who received adjuvant therapy, 42 patients switched to a second adjuvant regimen, and 5 patients switched to a third adjuvant regimen (Table 2). The most commonly used second adjuvant therapy regimen was also carboplatin and paclitaxel; the number of patients receiving a third adjuvant regimen was too small to identify the most common regimen.

A total of 68 patients received therapy after disease recurrence, and the most common regimen was carboplatin and paclitaxel (Table 2).

Health Care Resource Use and Cost

Billing and charge data during adjuvant treatment were available for 228 patients. A total of 407 patients had billing and charge data available at any time. Table 3 presents information on health care resource use by disease stage during adjuvant treatment and for the period from diagnosis up to the end of the first regimen after disease recurrence or end of the medical record (whichever occurred first). There were no statistically significant differences across disease stages in office visits, during adjuvant therapy, or from diagnosis to the end of the first regimen after disease recurrence or the end of medical record, or the incidence or duration of hospitalizations during adjuvant therapy (Table 3). In contrast, among patients who experienced recurrence, the frequency of hospitalization differed significantly across groups diagnosed at different stages of disease ($P = .0025$), but the duration of hospitalization did not significantly differ across groups diagnosed at different stages of disease ($P = .1280$).

Table 4 shows cost by disease stage during adjuvant treatment and for the period of diagnosis up to the end of the first regimen after disease recurrence or end of the medical record (whichever occurred first). During adjuvant treatment, the total monthly median cost per patient was $17,389.75 (interquartile range, $8,815.61-23,360.85) whereas the monthly cost from diagnosis until the end of the initial systemic therapy regimen after recurrence or the end of medical record was $1,185.08 (interquartile range, $250.60 to $2,535.99).

The mean overall cost of care during the entire duration of adjuvant treatment was $49,131.61 (SE $2,359.42). The mean overall cost from diagnosis until the end of the initial systemic therapy regimen after recurrence or end of medical record was $62,986.20 per patient (SE $16,846.85). Overall average costs by disease stage are shown in Figure 1.

Table 4 Cost of Care Per Month During Adjuvant Therapy as Well as From Diagnosis to the End of First Regimen After Disease Recurrence or End of Medical Record by Disease Stage

Category		Cost (US$) by Disease Stage				
During Adjuvant Therapy	**Statistic**	**IB (n = 63)**	**IIA/II (n = 52)**	**IIB (n = 48)**	**IIIA (n = 65)**	**Overall[b] (n = 228)**
Systemic chemotherapy	Median	$11,119.87	$13,970.99	$11,422.15	$9,211.14	$11,311.71
	IQR	$4,921.54-17,014.09	$6,963.59-16,869.85	$5,928.17-16,601.24	$4,075.24-15,641.38	$5,195.70-16,707.72
	n[c]	57	41	38	56	192
Targeted therapy	Median	$5,099.07	—	$7,498.29	—	$7,321.16
	IQR	$5,099.07-5,099.07	—	$7,144.02-7,636.08	—	$6,121.55-7,567.19
	n[c]	1	0	3	0	4
Infused supportive care drugs	Median	$4,909.07	$6,275.17	$4,402.89	$5,199.69	$5,338.42
	IQR	$1,884.89-7,540.52	$4,291.79-8,880.50	$1,676.67-8,877.58	$2,027.30-8,727.50	$2,134.44-8,669.44
	n[c]	30	20	22	25	97
Other drugs	Median	$1,854.30	$1,949.66	$1,754.20	$1,540.04	$1,795.94
	IQR	$1,276.21-2,578.76	$1,218.55-2,345.87	$1,153.72-2,563.63	$1,092.75-2,314.66	$1,146.13-2,533.75
	n[c]	58	42	41	57	198
Office visits	Median	$432.41	$362.58	$380.02	$403.50	$403.50
	IQR	$274.42-588.26	$265.15-509.97	$217.48-614.51	$302.16-553.48	$274.42-574.96
	n[c]	62	52	48	65	227
Other procedure costs	Median	$2,459.03	$2,060.30	$2,066.88	$2,370.16	$2,213.15
	IQR	$1,672.99-3,373.25	$1,338.41-2,764.36	$1,457.82-2,942.00	$1,886.47-3,011.05	$1,596.70-3,052.15
	n[c]	62	52	48	65	227
Total costs[a]	Median	$17,495.64	$19,178.60	$17,784.05	$13,659.36	$17,389.75
	IQR	$12,258.13-23,291.50	$6,798.71-22,463.90	$8,152.45-24,341.09	$9,807.96-23,735.01	$8,815.61-23,360.85
	n[3]	63	52	48	65	228
From Diagnosis to End of First Regimen After Disease Recurrence or End of Medical Record		**IB (n = 158)**	**IIA/II (n = 81)**	**IIB (n = 67)**	**IIIA (n = 101)**	**Overall (n = 407)**
Systemic chemotherapy	Median	$924.33	$1,084.64	$1,034.34	$1,035.61	$1,030.60
	IQR	$417.53-2,324.48	$770.54-1,648.74	$645.32-1,760.08	$387.40-2,662.71	$475.64-1,865.96
	n[c]	62	43	47	76	228
Targeted therapy	Median	$2,024.58	$9,651.00	$2,200.31	$1,875.88	$2,275.25
	IQR	$1,064.78-5,191.78	$9,651.00-9,651.00	$1,691.80-3,486.52	$488.02-3,294.31	$1,064.78-4,447.11
	n[c]	5	1	4	4	14
Infused supportive care drugs	Median	$652.58	$671.85	$441.28	$422.80	$515.22
	IQR	$218.59-1,191.98	$396.08-974.85	$257.43-677.28	$271.31-1,135.91	$257.43-1,070.18
	n[c]	35	20	29	29	113

Table 4 Continued

From Diagnosis to End of First Regimen After Disease Recurrence or End of Medical Record		IB (n = 158)	IIA/II (n = 81)	IIB (n = 67)	IIIA (n = 101)	Overall (n = 407)
Other drugs	Median	$128.74	$166.66	$180.39	$204.66	$165.55
	IQR	$28.73-247.95	$86.36-303.98	$95.53-245.85	$108.14-433.90	$76.32-306.02
	n[c]	94	50	54	82	280
Office visits	Median	$81.82	$103.51	$115.02	$143.08	$105.45
	IQR	$50.42-161.33	$65.38-196.54	$63.74-207.47	$68.08-281.54	$57.81-207.52
	n[c]	157	81	67	101	406
Other procedure costs	Median	$205.34	$276.42	$366.86	$423.65	$285.79
	IQR	$55.47-440.14	$94.86-609.99	$169.94-628.98	$161.88-789.05	$96.22-596.15
	n[c]	146	78	66	99	389
Total costs[a]	Median	$495.22	$1,368.32	$1,713.95	$1,578.55	$1,185.08
	IQR	$128.43-1,570.08	$248.16-2,210.36	$719.10-2,964.43	$734.18-3,837.78	$250.60-2,535.99
	n[3]	158	81	67	101	407

Abbreviation: IQR = interquartile range.
[a]Total costs of care are defined as the sum of the costs of systematic/targeted therapy, infused supportive care drugs, other drugs, office visits, and other procedure costs.
[b]No formal comparisons on cost data were conducted.
[c]Includes patients who incurred at least 1 cost.

NSCLC Recurrence After Resection

Overall, approximately three-quarters (75.7%, 461 of 609) of patients did not have evidence of disease recurrence in their medical charts. A total of 87 patients had a distant recurrence, and 61 had a local or regional recurrence. Although there were no statistically significant differences in disease recurrence by disease stage (P = .0908), there appeared to be a trend in which there was a higher likelihood of disease recurrence, especially distant disease recurrence, with more advanced stage at diagnosis. In patients who had disease recurrence, the median time to recurrence was 12.56 months. There was a trend to shorter time to recurrence with more advanced disease stage, although this did not reach statistical significance (P = .2208) (Table 5).

Kaplan-Meier Analyses

Table 6 shows the results of Kaplan-Meier analyses of the total duration of adjuvant therapy (all regimens), duration of the initial regimen after disease recurrence, and disease-free survival by disease stage. There were no statistically significant differences across disease stages in the duration of adjuvant therapy or the duration of initial therapy after disease recurrence. There was a difference in disease-free survival time by disease stage. The log rank test for this analysis was statistically significant (P = .0125), with consistently shorter median disease-free survival time for patients with more severe disease at diagnosis compared to earlier disease stages.

Early Versus Late Treatment Start Date

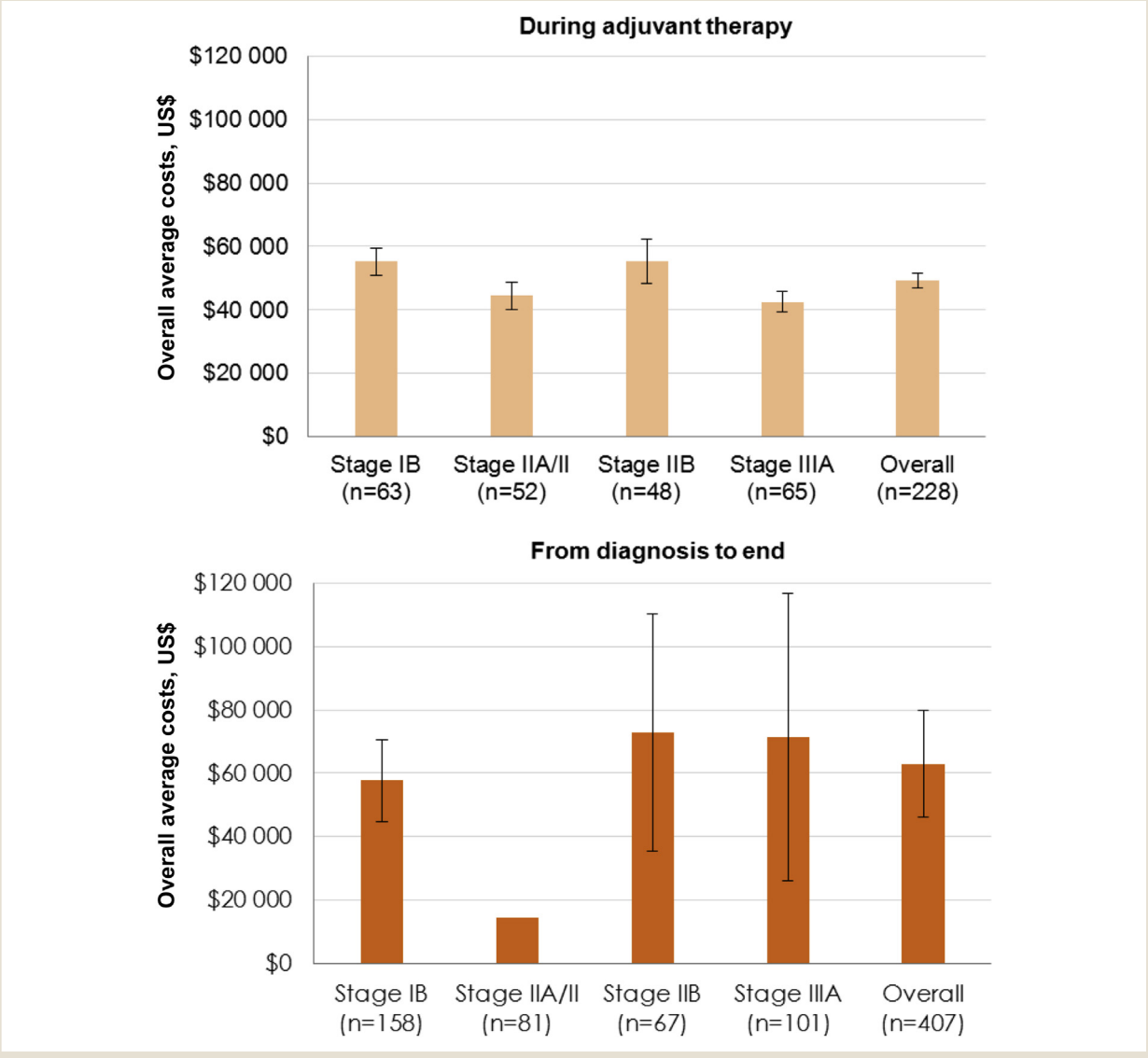
Treatment start dates were recorded for 594 patients (data were missing for 15 patients [date of diagnosis, 12 patients; date of start of treatment, 3 patients]). Of these, 165 patients had a record of an early start date for adjuvant treatment, 168 patients had a late adjuvant treatment start date, and 261 patients did not receive adjuvant therapy. There were no significant differences between the groups in terms of gender, race, minority status, or region of residence (all $P > .05$). There were statistically significant differences across groups for all of the clinical characteristics measured except for type of resection (P = .0564).

The most common first adjuvant regimen (ie, combined carboplatin and paclitaxel) was provided more frequently in patients with a late treatment start date (32.7%) than in patients with an early treatment start date (26.1%). Conversely, the second most common regimen, cisplatin, was provided more frequently in patients with an early treatment start date (17.6%) than in patients with a late treatment start date (10.3%).

Discussion

National Comprehensive Cancer Network (NCCN) guidelines recommend considering adjuvant therapy after surgery for patients with high-risk stage IB and II NSCLC, and they also recommend adjuvant systemic chemotherapy for all stage IIIA disease after surgery.[9] Until now, there has been little information available about the extent to which adjuvant therapy is used in routine practice by physicians in community oncology practices in the US. The present study reported that adjuvant therapy was used in 39.1% of patients with stage IB disease at diagnosis, increasing to approximately two-thirds of patients with stage II to IIIA disease. The recommended regimens for adjuvant chemotherapy in the

Figure 1 Overall Average Cost of Care Per Patient During Adjuvant Therapy and From Diagnosis to End of First Regimen After Disease Recurrence or End of Medical Record by Disease Stage



NCCN guidelines are cisplatin-based, with carboplatin and paclitaxel recommended for patients with comorbidities or patients who cannot tolerate cisplatin.[9] Consistent with the most recent guidelines, the most common regimens used for adjuvant therapy in this study were platin-based chemotherapy regimens such as cisplatin, cisplatin and docetaxel, cisplatin and vinorelbine, and carboplatin and paclitaxel. There was very little use of newer targeted therapies, which may reflect the patient population, as targeted therapies are typically used in advanced disease. Few patients were tested for biomarkers. The only biomarker tested in more than 10% of patients overall was EGFR, and almost 82% of tested patients were reported to be EGFR negative.

A study in Canada analyzed data from over 6,000 patients in the Ontario Cancer Registry who underwent resection for NSCLC to evaluate the uptake of adjuvant chemotherapy.[10] This study reported an increase in adjuvant chemotherapy use from 7% in 2001-2003 to 31% in 2004-2006.[10] The rate of adjuvant therapy use in the current study was higher than those reported in the Canadian study, with 56.7% of patients receiving adjuvant therapy overall. This could be consistent with a continuation of the increasing trend observed in the Canadian study, because the present study was conducted in a later time period (2007-2014), or could reflect country-specific differences in practice. It could also reflect population differences between the studies; for example, the Canadian study was conducted in the general population and the NSCLC stage was unknown in most of the patients, whereas in the present study the NSCLC stage was precisely defined and the population was drawn from a network of community oncology practices. In the Canadian study, 82% of patients with available information on the drug regimen received cisplatin and 17%

Table 5 Recurrence of NSCLC After Resection by Disease Stage

Variable/Statistic	Disease Stage					*P*
	IB (n = 215)	IIA/II (n = 130)	IIB (n = 110)	IIIA (n = 154)	Overall (n = 609)	
Recurrence, n (%)						.0908[a]
Yes	43 (20.0%)	29 (22.3%)	28 (25.5%)	48 (31.2%)	148 (24.3%)	
No	172 (80.0%)	101 (77.7%)	82 (74.5%)	106 (68.8%)	461 (75.7%)	
Overall	215	130	110	154	609	
Time to Recurrence, months						.2208[b]
Median	14.33	12.82	11.31	10.68	12.56	
Range	3.78-61.64	1.61-62.40	1.94-65.16	0.82-71.54	0.82-71.54	

Abbreviation: NSCLC = non–small cell lung cancer.
[a]Chi-square test.
[b]Kruskal-Wallis test.

received carboplatin.[10] In the present study, carboplatin use was higher; almost 30% of patients receiving adjuvant therapy received carboplatin and paclitaxel.

A study, published in 2013, analyzed data from a community oncology database in the US on patients with stage I to IV NSCLC who had started adjuvant or neoadjuvant therapy for early stage disease, or first-line therapy for advanced disease in 2009-2010.[11] Consistent with the present study, regimens based on carboplatin and paclitaxel were the most commonly used.[11] Another study in the US investigated NSCLC chemotherapy treatment at 8 community oncology practices, but the majority of patients in this study had advanced disease (72% stage IIIB to IV),[12] so the population differed substantially from that in the present study.

Our study has a number of limitations. First, it reflects treatment patterns only within community oncology practices that are part of the Vector Oncology Data Warehouse network, and it is possible that the Vector Oncology Data Warehouse patient population may not be representative of the general population of US NSCLC

Table 6 Kaplan-Meier Analysis of Duration of Adjuvant Therapy, Duration of Initial Therapy After Disease Recurrence, and Disease-Free Survival

Stage	Patients	Events	Estimate (Median/First Quartile)[a]	Lower 95% CI	Upper 95% CI	Log Rank *P* Value
Duration of Adjuvant Therapy, months						.5197
IB	84	84	2.80	2.80	2.96	
IIA/II	86	86	2.80	2.80	2.86	
IIB	75	75	2.80	2.80	2.99	
IIIA	100	100	2.80	2.76	2.80	
Overall[b]	345	345	2.80	—	—	
Duration of Initial Regimen After Disease Recurrence, months						.1523
IB	17	17	2.30	1.87	4.18	
IIA/II	15	15	2.86	1.41	4.64	
IIB	13	13	1.41	0.72	1.87	
IIIA	23	23	2.80	1.71	4.14	
Overall	68	68	2.20	1.87	3.26	
Disease-Free Survival Time, months[c]						.0125
IB	209	39	42.06	19.83	—	
IIA/II	128	27	39.13	13.65	—	
IIB	109	28	22.72	13.02	63.12	
IIIA	151	45	12.20	7.14	20.45	
Overall	597	139	23.38	17.56	40.32	

Abbreviation: CI = confidence interval.
[a]Median values are presented for durations. For disease-free survival, instead of the median values, the first quartile (75% survival rate) values are reported because the median could not be estimated uniformly across all stage subgroups.
[b]Confidence interval could not be calculated, likely due to a large number of ties at the median value.
[c]Survival time could not be calculated for 12 patients as a result of missing date of resection.

patients or of treatment patterns in other practices. For example, biomarker testing may differ in academic centers compared to community settings. Second, this was a retrospective study conducted using patient data from 2007 to 2014, and future treatment patterns may change with the advent of newer treatments in NSCLC. Third, the cost analysis was based on patient charge data, which were not available for all the patients in the sample and may not reflect the actual costs incurred. Some costs, such as hospitalizations, occurred outside community oncology and thus were not captured in the study. Fourth, the follow-up time varied between patients, because the study period extended until the end of the first therapy regimen after disease recurrence or the end of the medical record, whichever occurred first. Fifth, data on some parameters may not be consistently available from the patient records in Electronic Medical Record data sources, including those from the Vector Oncology Data Warehouse.

To our knowledge, this is the first study conducted in the US of community oncology practice patterns in patients with resected stage IB to IIIA NSCLC. As such, it provides an insight into treatment patterns and costs in real-world clinical practice. However, this study only investigated treatment patterns and did not attempt to compare real-world outcomes such as disease-free and overall survival between patients with resected NSCLC who received adjuvant therapy and those who did not receive it. This would be a potentially interesting area for future research.

Conclusion

In this real-world study of community oncology treatment of patients with resected NSCLC in the US, adjuvant systemic therapy was provided in some patients with stage IB NSCLC and in the majority of patients with stage IIA to IIIA disease. Most patients had no record of biomarker testing, and targeted therapies were little used. The most common adjuvant regimens were based on traditional chemotherapy agents such as carboplatin and cisplatin. There were few differences in regimen or health care resource use by disease stage.

Clinical Practice Points

- Complete surgical resection is the standard treatment for early stage NSCLC; however, disease still recurs in a high proportion of patients. Adjuvant chemotherapy can help to reduce the risk of recurrence after surgery and has demonstrated survival benefits in clinical trials.
- Current NCCN guidelines recommend considering adjuvant therapy after surgery for patients with high-risk stage IB and II NSCLC and also recommend adjuvant systemic chemotherapy for all stage IIIA disease.
- A retrospective observational analysis of electronic medical records collected during routine care at US community oncology sites between January 2007 and January 2014 included 609 patients with resected stage IB to IIIA disease; adjuvant systemic therapy after resection was provided to 56.7% of patients overall, with significantly lower use in patients with stage IB disease (39.1%) than stage II to IIIA disease (64.9-68.2%).
- The most common adjuvant regimen at all stages was the combination of carboplatin and paclitaxel. This study provides timely information about the extent to which adjuvant therapy is used in routine practice by physicians at US community oncology practices. Adjuvant systemic therapy was used in some patients with stage IB NSCLC and in a majority of patients with stage IIA to IIIA disease; the most common therapies utilized were platin-based chemotherapy regimens.
- Although factors such as performance status, comorbidities, and patient preference were not directly assessed, these results suggest that community oncologists in the US are using adjuvant treatment in a manner consistent with the NCCN guidelines.

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Disclosure

POB and BA are employees of the GSK group of companies and hold restricted shares from GSK plc. KRS, MSW and PJEM report fees for services to their institution from the GSK group of companies during the conduct of the study and outside the submitted work.

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