

Understanding Total Cost of Care in Advanced Non-Small Cell Lung Cancer Pre- and Postapproval of Immuno-Oncology Therapies

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Lung cancer is the second most common cancer and the leading cause of cancer-related mortality in the United States, with approximately 234,030 new cases and 154,050 deaths expected in 2018.¹ Approximately 85% of all lung cancer cases are classified as non-small cell lung cancer (NSCLC), and more than half (57%) of incident cases present at an advanced stage.¹⁻² The prognosis for patients with advanced NSCLC (aNSCLC) has been historically poor. Five-year relative survival is less than 5% on standard treatments including surgery, radiation, and systemic antineoplastic therapy (ST), primarily in the form of platinum-based chemotherapy.^{1,3}

The development of mutation-targeting and immuno-oncology (IO) drugs is revolutionizing the treatment and prognosis of NSCLC. Since 2011, 4 agents targeting anaplastic lymphoma kinase and 5 agents targeting the epidermal growth factor receptor have been approved by FDA for NSCLC.⁴⁻¹² Each agent received a salvage indication, and 6 of those received a frontline indication. The March 2015 approval of the first IO agent, nivolumab, for patients with aNSCLC, heralded a new era in treatment. Since 2015, 2 additional IO agents have been approved for patients with NSCLC with a salvage indication: pembrolizumab as frontline therapy and durvalumab as an adjuvant therapy.¹³⁻¹⁹ In 2016, the Institute of Clinical and Economic Review (ICER) commenced a cost-effectiveness analysis that demonstrated the value of novel therapies, such as IO, in both frontline and second-line NSCLC. ICER did note higher-than-acceptable cost per quality-adjusted life-year (QALY) gained. In the same report, cost per QALY for targeted therapies was considered acceptable in their approved indications.²⁰

The published literature suggests that NSCLC is the fifth costliest tumor in the United States, with an estimated 2016 national expenditure of approximately \$13.6 billion.²¹ Although much attention has been paid to drug costs, particularly costs of IO therapies, there has been no research to understand the real-world healthcare resource utilization (HRU) and associated total cost of care in the period prior to IO approval in NSCLC compared with the period when IO agents have emerged as effective treatment options. Most of the published real-world evidence in NSCLC is based on older data

ABSTRACT

This study assesses resource utilization and total direct medical cost among patients in the United States starting systemic antineoplastic therapy (ST) pre- and postapproval of immuno-oncology (IO) agents for advanced non-small cell lung cancer. Adults diagnosed with lung cancer initiating first-line ST within 6 months of diagnosis during either the pre- (March 2013-March 2014) or post-IO (March 2015-December 2016) approval period were identified in a US-based multipayer administrative claims database. Excluded were patients with small cell lung cancer, secondary malignancies, less than 1 month follow-up, and those in clinical trials. Total cost (TC) was calculated from the date of initiation of treatment until the last follow-up. Propensity score matching was adjusted for differences in patient cohorts, including follow-up time. Binary multiple logistic regression assessed predictors of high TC (above mean) pre- and post IO. Mean TC per patient was higher pre-IO versus post IO in both unmatched (\$165,548 vs \$95,715) and matched analyses (\$129,977 vs \$113,177). Hospitalization and emergency department (ED) visit rates were higher pre-IO versus postapproval. Predictors of high TC pre-IO included use of first-line combination therapy, radiation, targeted therapy, maintenance therapy, biomarker testing, more comorbidities, longer follow-up, first-line hospitalization, first-line cost above mean, and age 65 years and older. In the post-IO period, additional predictors of higher TC included use of IO, having mild liver disease or hemiplegia, and longer time to ST initiation. Early data show lower ED visit and hospitalization rates and associated lower TC in the post-IO era.

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For author information and disclosures, see end of text.

reporting patterns of care and costs prior to the approval of targeted and IO therapies. In addition, many of the published findings are not generalizable, as they represent a single institution, focus on a patient subgroup such as elderly or early-stage patients with NSCLC, or include patients not treated with ST.²²⁻²⁶ Many studies also focus on chemotherapy costs alone, with little information presented regarding broader treatment patterns, resource use, and costs for other services incurred by patients with NSCLC.²⁵⁻²⁷ Current real-world studies are needed to evaluate the relative impact of new drug treatment strategies on total cost and HRU among patients with aNSCLC to understand the value of various treatment choices for this difficult-to-treat population.

To address this knowledge gap, the primary objective of this research is to evaluate HRU rates and total cost (TC) of care from a US payer perspective among patients with aNSCLC treated with ST in the time periods before and after approval of these agents for treatment (pre-IO and post-IO periods, respectively). The secondary objective is to identify predictors of high treatment costs among patients with aNSCLC treated in the pre- and post-IO approval periods.

Methods

Study Design

The target population for the study included patients diagnosed with lung cancer who initiated treatment with NSCLC-specific ST between March 1, 2013, and December 31, 2016, and followed through March 2017, with history back to March 2012. Two independent, mutually exclusive patient cohorts were selected based on the time of initiation of ST for aNSCLC: cohort 1 (pre-IO period) included patients initiating first-line treatment between March 1, 2013, and February 28, 2014; cohort 2 (post-IO period) included patients initiating first-line treatment between March 1, 2015, and December 31, 2016. The index period for the post-IO period was longer than that for the pre-IO period to increase the number of patients who had received IO therapy. Patients initiating first-line treatment between March 1, 2014, and February 28, 2015, were excluded. This 1-year washout period was used to isolate the period before the introduction of IO and to minimize the effect of patient crossover between the 2 cohorts. Patients with aNSCLC were identified within the Medical Outcomes Research for Effectiveness and Economics Registry Research database, composed of multipayer claims data from 243 million unique patients since 2000.² The information represents adjudicated medical and pharmacy claims from traditional fee-for-service commercial plans, Medicare Advantage, Managed Medicare, Medicaid, and dual-eligible plans.²⁸ A dataset containing records from March 2012 through March 2017 was available at the time of data acquisition.

Patient Selection Criteria

All individuals with at least 1 nondiagnostic inpatient or outpatient claim for lung cancer (*International Classification of Diseases,*

Ninth Revision [ICD-9] and Tenth Revision [ICD-10] codes: 162.XX/C34.XX) who were 18 years or older at the time of the first lung cancer claim or diagnosis date were selected. Patients were considered to have developed advanced disease (IIIB or IV) if they received their first ST within 6 months of the lung cancer diagnosis or had secondary metastases codes at diagnosis (ICD-9: 196.XX, 197.XX, 198.XX; ICD-10: C77.XX, C78.XX, C79.XX). Next, a longitudinal record of patient treatment history was constructed from pharmacy and medical claims using National Drug Codes (NDC) numbers and J codes. Only patients who had newly initiated (no treatment in the prior 12 months) NSCLC treatment with a regimen recommended by the National Comprehensive Cancer Network (NCCN) during the pre- or post-IO index periods were included. Treatment regimens and a line of therapy assignment were based on group-administered chemotherapies using administration dates. Line of therapy determination was made using the following process: antineoplastic agents administered within 30 days of each other were considered combination therapy; change in regimen (use of new agents, addition of an agent, or discontinuation of an agent in a regimen for at least 60 days), or a regimen gap of more than 12 weeks triggered a line-of-therapy increment. Maintenance therapy was defined per NCCN guidelines as erlotinib, bevacizumab, pemetrexed, docetaxel, or gemcitabine within 6 weeks of first-line ST initiation, provided first-line was a platinum-based or pemetrexed-based combination given for at least 4 cycles. All patients were required to have a minimum of 1 month follow-up from the date of initiation of the first-line treatment.

As ICD-9/10 codes do not distinguish between NSCLC and small cell lung cancer (SCLC), patients were excluded from the analysis if they received a treatment consistent with NCCN guidelines for SCLC (eg, topotecan, temozolomide, cranial irradiation). Additionally, patients with a second primary cancer diagnosis or those who received care as part of a clinical trial (ICD-9: V70.7; ICD-10: Z00.6) were excluded.

Resource Utilization and Costs

Acute care interventions were identified using admission codes for hospitalizations and emergency department (ED) visits. The average wholesale price for drugs coded with NDC codes and CMS and the average sales price for drugs coded with J, Q, or C codes were used to calculate standardized cost per administration of any antineoplastic agent or other pharmaceutical. The CMS clinical laboratory fee schedule, Medicare physician fee schedule, and hospital outpatient prospective payment system were used to standardize procedure costs. Facility fees for acute care admissions per day for each evaluation period were calculated using actual paid amounts and multiplied by length of stay. All costs were adjusted to 2017 US dollars.

Data Analysis

HRU, TC, and TC per patient per month (PPPM) were compared between the pre-IO and post-IO cohorts for all lines of therapy

combined and per line of therapy. TC, TC PPM, and HRU by line of therapy were calculated from the first administration of ST for a given line until the beginning of the next line of therapy or last available claim if there was no subsequent treatment. Costs and HRU for third-line treatment or higher were presented as third-line-plus. Mean costs were reported for those patients utilizing the resource (ie, inpatient, ED, and ST), whereas mean TCs were calculated across all patients.

Comparisons between pre-IO and post-IO HRU costs were conducted between all patients (unmatched) and a subgroup of propensity score matched (PSM) patients. The PSM method was used to control the differences in demographic and clinical characteristics of the patient cohorts, such as age, gender, site(s) of metastases, geographic region, comorbidities, smoking status, payer type, and the length of follow-up. The χ^2 test or Fisher Exact test were used to assess differences between cohorts for categorical variables, and the *t* test was used to evaluate differences in continuous variables.

Multivariable binary logistic regression was used to assess predictors of high TC in each of the pre- and post-IO cohorts. Since the introduction of IO was expected to influence TC in the treatment lines where it is used most frequently, predictors of TC in second-line treatment were also assessed. For the predictive model, high cost was defined as TC above the mean per period. Evaluated predictors included:

- Gender
- Payer type
- First-line combination therapy (vs monotherapy)
- Maintenance therapy
- Radiation therapy
- Surgery
- Biomarker testing
- History of smoking or smoking cessation (receipt of smoking counseling, chronic obstructive pulmonary disease or emphysema diagnosis, or use of smoking cessation drugs)
- Presence of individual comorbidities included from the Charlson Comorbidity Index (CCI)
- CCI score >2
- Age at time of treatment start (<65 or ≥65 years)
- Drug class (targeted therapy, chemotherapy, or IO)
- Hospitalization or ED visit in first-line
- Cost above mean in first-line

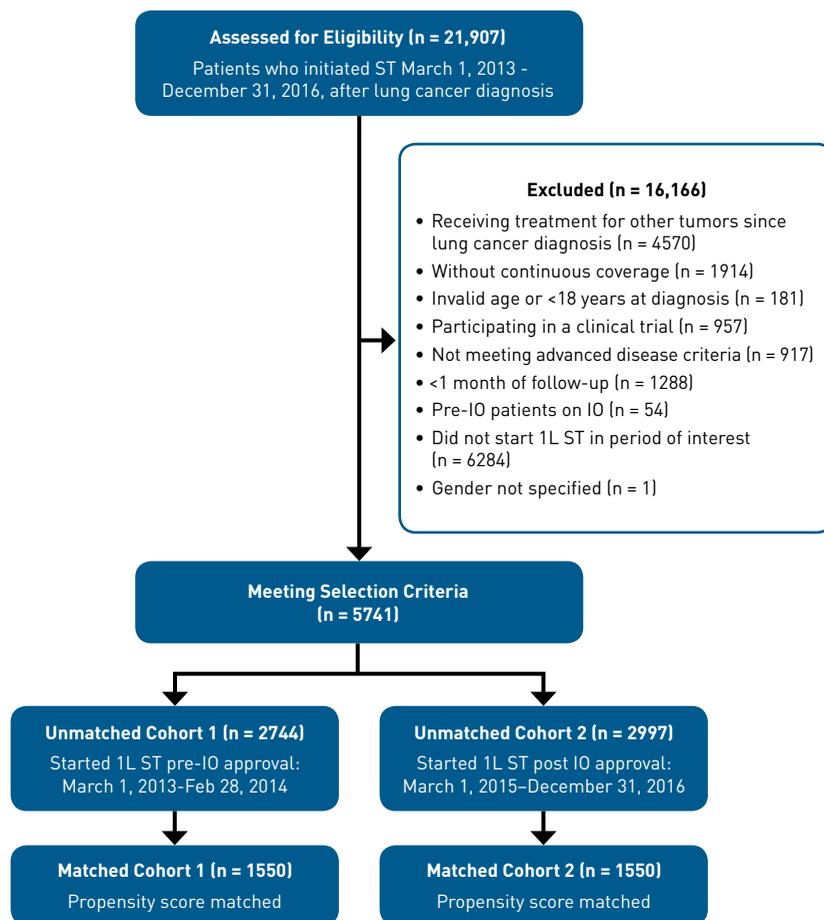
- Hospitalization or ED visit in any line of therapy
- Time to treatment start (months)
- Time to first-line discontinuation (months)
- First-line adverse event count
- Length of follow-up (months)

All analyses were conducted using SPSS (version 22.0, IBM Corporation, Armonk, New York); *P* < .05 was considered significant.

Results

A total of 21,907 individuals with a lung cancer diagnosis had received ST, and of these, 5741 met eligibility criteria, including 2744 (48%) and 2997 (52%) who initiated first-line treatment in the pre-IO and post-IO periods, respectively (Figure 1). Demographic and baseline clinical characteristics for the unadjusted and matched patient cohorts are presented in Table 1. Patients in the unmatched post-IO cohort were older, more likely to be male, had a higher CCI

FIGURE 1. Study Eligibility Breakdown



1L indicates first-line; IO, immuno-oncology; ST, systemic antineoplastic therapy.

TABLE 1. Patient Demographic and Clinical Characteristics in the Pre-IO and Post-IO Cohorts

	Unmatched Cohorts					Matched Cohorts				
	Cohort 1 Pre-IO n = 2744		Cohort 2 Post IO n = 2997		P	Cohort 1 Pre-IO n = 1550		Cohort 2 Post IO n = 1550		P
Male (n, %)	1259	46%	1486	50%	.005	746	48%	744	48%	.943
Payer type (n, %)	<.001					.019				
Commercial	722	26%	560	19%		386	25%	381	25%	
Medicaid	539	20%	634	21%		293	19%	355	23%	
Medicaid, Medicare	0	0%	7	0%		0	0%	0	0%	
Medicare	1256	46%	1689	56%		871	56%	814	53%	
Unknown	227	8%	107	4%		0	0%	0	0%	
US region (n, %)	<.001					<.001				
Northeast	428	16%	456	15%		247	16%	251	16%	
South	763	28%	597	20%		437	28%	295	19%	
Central	951	35%	1474	49%		520	34%	787	51%	
West	602	22%	470	16%		346	22%	217	14%	
History of smoking (n, %)	969	72%	1987	66%	<.001	1109	72%	1097	71%	.634
Age at treatment start (years; mean, SD)	64.6	10.9	66.4	10.5	<.001	65.7	10.9	65.4	10.4	.503
Sites of metastasis (n, %)										
Bone metastases	421	15%	331	11%	<.001	237	15%	240	15%	.881
Brain metastases	277	10%	232	8%	.002	157	10%	154	10%	.858
Liver metastases	216	8%	173	6%	.001	111	7%	117	8%	.680
Lymph nodes	547	20%	489	16%	<.001	310	20%	310	20%	1.000
Adrenal gland	86	3%	66	2%	.029	48	3%	48	3%	1.000
Visceral metastases	542	20%	456	15%	<.001	297	19%	306	20%	.683
Charlson Comorbidity Index score (mean, SD)	2.2	2.8	2.4	3.0	.013	2.3	2.9	2.2	2.9	.515
Number of comorbidities per patient (mean, SD)	1.0	1.3	1.0	1.4	<.001	1.0	1.3	1.0	1.3	.456
Months follow-up from treatment start (mean, SD)	16.9	10.7	8.9	5.5	<.001	11.4	6.2	11.3	5.7	.650
Total lines of therapy (mean, SD)	1.9	1.1	1.4	0.8	<.001	1.8	1.0	1.6	0.9	<.001
Any treatment with IO therapy (n, %)	0.0	0.0%	432	14.4%	—	0.0	0.0%	264	17.0%	—

IO indicates immuno-oncology; SD, standard duration.

score, received fewer lines of therapy, and were more likely to have no history of smoking, as compared with those in the unmatched pre-IO cohort. Mean length of follow-up was 16.9 months for the pre-IO and 8.9 months for the post-IO cohort ($P < .001$). Among the patients receiving IO, 63% (271 of 432) received IO in second-line. PSM resulted in 2 matched cohorts of 1550 patients for the pre- and post-IO groups. Age, gender, smoking status, comorbidity score, and mean length of follow-up were not significantly different. However, several variables, including number of lines of therapy received, payer type, and region of residence remained significantly different (Table 1).

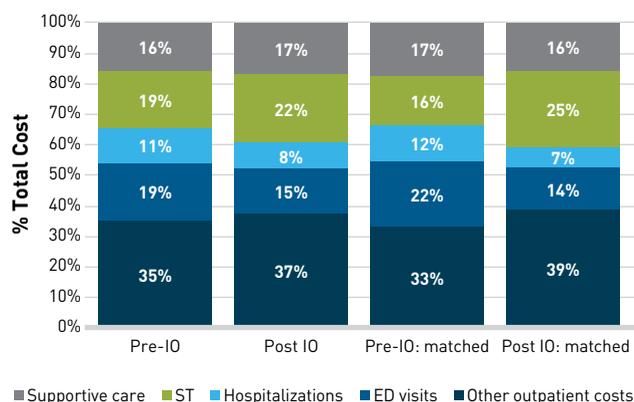
Table 2 lists HRU and cost comparisons for all lines combined for both matched and unmatched cohorts. In the matched cohort analysis, the observed proportion of patients experiencing a hospitalization in the pre-IO versus post-IO cohort was 61% and 46% ($P < .001$), respectively, while the rate of ED visits was 77% in the pre-IO versus 66% in the post-IO cohort ($P < .001$). The mean TC in the pre-IO cohort was \$129,977 compared with \$113,117 in the post-IO cohort ($P < .001$). ST costs represented 16% of pre-IO TC compared with 25% of post-IO TC; hospitalization costs were 12% versus 7%, and ED visit costs were 22% versus 14% of TC, for pre-IO TC and post-IO TC, respectively (Figure 2). By line of therapy, TCs were

TABLE 2. Healthcare Resource Utilization and Cost Comparison for the Entire Follow-up Period Between Pre- and Post-IO Cohorts Unmatched and Matched

	Unmatched Cohorts			Matched Cohorts		
	Cohort 1 Pre-IO n = 2744	Cohort 2 Post IO n = 2997	P	Cohort 1 Pre-IO n = 1550	Cohort 2 Post IO n = 1550	P
Any hospitalization (n, %)	1678 (61)	1353 (45)	<.001	946 (61)	713 (46)	<.001
Hospitalizations (mean, SD)	2.5 (2.1)	2.0 (1.5)	<.001	2.3 (1.6)	2.1 (1.7)	.006
LOS (mean, SD)	1.9 (4.3)	2.2 (9.5)	.159	1.7 (2.7)	2.1 (8.4)	.155
Any ED visit (n, %)	2145 (78)	1896 (63)	<.001	1194 (77)	1016 (66)	<.001
ED visits, mean (SD)	3.7 (4.4)	2.7 (2.5)	<.001	3.3 (3.0)	2.9 (2.6)	.002
Total cost of care (mean, SD)	\$165,548 (\$153,049)	\$95,715 (\$90,337)	<.001	\$129,977 (\$112,479)	\$113,117 (\$96,557)	<.001
ED visit cost	\$40,281 (\$61,000)	\$22,764 (\$31,091)	<.001	\$36,639 (\$50,541)	\$23,331 (\$27,065)	<.001
Hospitalization cost	\$29,924, (\$84,072)	\$17,459 (\$51,412)	<.001	\$24,876, (\$61,778)	\$17,680 (\$56,115)	<.013
ST cost	\$31,487 (\$62,644)	\$21,599 (\$39,940)	<.001	\$21,025 (\$38,531)	\$27,928 (\$48,566)	<.001
Per patient per month total cost of care (mean, SD)	\$11,522 (\$9580)	\$11,977 (\$8763)	.060	\$12,681 (\$10,371)	\$10,758 (\$7221)	<.001

ED indicates emergency department; IO, immuno-oncology, LOS, length of stay; SD, standard duration; ST, systemic antineoplastic therapy.

FIGURE 2. Distribution of Inpatient and Outpatient Costs*



ED indicates emergency department; IO, immuno-oncology; ST, systemic antineoplastic therapy.

*Due to rounding proportions, percentages may not add to 100%.

statistically significantly lower in the post-IO cohort during first-line therapy (\$80,206 vs \$87,890; $P = .011$) but were not significantly different in the second-line or third-line-plus groups (Table 3).

Figures 3a and 3b depict the results of the multivariable logistic regression model for predictors of high TC in matched pre- and post-IO cohorts, respectively. The forest plot shows significant predictors ranking from the highest to the lowest odds of having TC above the mean. Significant predictors of TC above the mean among aNSCLC patients in the pre-IO period were the use of first-line combination therapy; receipt of radiation therapy, targeted therapy, or maintenance therapy; evidence of biomarker testing;

having a CCI score >2; diabetes at diagnosis; longer follow-up time; first-line hospitalization; having first-line TC cost above the mean; and being aged ≥65 years at ST initiation. Post IO, predictors of high TC were similar to those in the pre-IO period. In addition to receiving targeted therapy versus chemotherapy, high TC predictors in the post-IO period included receiving IO therapy versus chemotherapy, having mild liver disease or hemiplegia at diagnosis, and longer time to initiation of first-line treatment. In both the pre- and post-IO periods, the highest odds of TC above the mean in all lines of therapy was attributed to higher TC during first-line treatment.

Significant predictors of second-line TC above the mean (Figure 3c) in the pre-IO period were evidence of smoking, receipt of second-line targeted therapy, ED visit, hospitalization during second-line treatment, or longer follow-up. Predictors of second-line TC equal to or below the mean included male sex, aged ≤65 years at first-line initiation, maintenance use, or an ED visit during first-line treatment. In the post-IO cohort, patients with mild liver disease at diagnosis; those receiving second-line IO or targeted therapy; those having an ED visit or hospitalization during second-line treatment; or those with longer follow-up were more likely to have higher second-line TC. However, those with a shorter time to first-line discontinuation or who were aged <65 years were less likely to have higher second-line TC (Figure 3d). The highest odds of having higher TC among the pre-IO cohort were attributed to second-line targeted therapy use and to second-line ED visits. The highest odds in the post-IO were attributed to second-line targeted therapy, followed by evidence of mild liver disease at diagnosis.

TABLE 3. Healthcare Resource Utilization and Costs Comparison Between Pre-IO and Post-IO Cohorts by Line of Therapy Matched

	Cohort 1 Pre-IO 1L (n = 1550)	Cohort 2 Post IO 1L (n = 1550)	P	Cohort 1 Pre-IO 2L (n = 734)	Cohort 2 Post IO 2L (n = 568)	P	Cohort 1 Pre-IO 3L+ (n = 377)	Cohort 2 Post IO 3L+ (n = 259)	P
Months of follow-up (mean, SD)	7.9 (5.6)	8.6 (5.6)	.001	5.0 (4.2)	5.3 (4.5)	.162	3.8 (3)	4.2 (3.7)	.111
Any hospitalization (n, %)	689 (44.4%)	576 (37.2%)	<.001	314 (42.8%)	170 (30.0%)	<.001	148 (39.3%)	79 (30.5%)	.024
Hospitalizations (mean, SD)	2 (1.4)	1.8 (1.3)	.051	1.7 (1.1)	1.7 (1.3)	.818	1.6 (0.8)	1.5 (1.2)	.874
LOS (days; mean, SD)	1.8 (3.3)	1.9 (3.6)	.592	1.6 (0.5)	2.8 (15.9)	.182	1.6 (0.6)	1.7 (0.7)	.428
Any ED visit (n, %)	914 (59.0%)	854 (55.1%)	.029	420 (57.2%)	257 (45.2%)	<.001	194 (51.5%)	122 (47.1%)	.281
ED visits, mean (SD)	2.7 (2.4)	2.5 (2)	.055	2.2 (1.9)	2.2 (1.8)	.601	2.2 (2)	2.1 (1.6)	.682
Total costs of care per line of therapy (mean, SD)	\$87,890 (\$96,925)	\$80,206 (\$69,033)	.011	\$57,183 (\$59,243)	\$61,662 (\$86,524)	.291	\$50,166 (\$51,234)	\$54,997 (\$56,485)	.272
ED visit costs	\$30,236 (\$44,805)	\$20,432 (\$22,600)	<.001	\$17,014 (\$21,042)	\$19,785 (\$107,104)	<.001	\$25,775 (\$29,807)	\$15,112 (\$14,857)	<.001
Hospitalization costs	\$22,296 (\$69,506)	\$14,406 (\$20,981)	.009	\$24,127 (\$33,023)	\$16,364 (\$19,063)	.739	\$16,120 (\$17,851)	\$10,740 (\$8546)	.012

1L indicates first-line; 2L, second-line; 3L, third-line; ED, emergency department; IO, immuno-oncology; LOS, length of stay; SD, standard duration.

Discussion

Over the past 30 years, rates of smoking and lung cancer incidence in US men have diminished dramatically. Yet, lung cancer remains the second most common cancer after breast cancer and remains the leading cause of cancer mortality. This human tragedy is further aggravated by the financial burden it causes for patients and society, with costs of more than \$300 billion each year, including \$156 billion in direct medical care costs.²⁹ After 3 decades of research, during which the limited arsenal of systemic chemotherapy and radiation treatments have had minimal impact on the overall survival of patients with aNSCLC, optimism now abounds as new drug classes offer hope—but at what cost? Limited data exist regarding the cost of treating aNSCLC in the United States, and regarding the changes in cost and HRU before and after the approval of the IO drug class. This is the first study to evaluate HRU and total costs of care among patients with aNSCLC pre- versus post IO approval. Although the proportion of TC attributed to ST grew in the post-IO period, our study showed an overall decrease in TC, as well as a lower rate of hospitalizations and ED visits among patients receiving ST in the post-IO period versus a demographically and clinically matched pre-IO cohort. These findings suggest that the availability of IO agents has not increased total spending for aNSCLC.

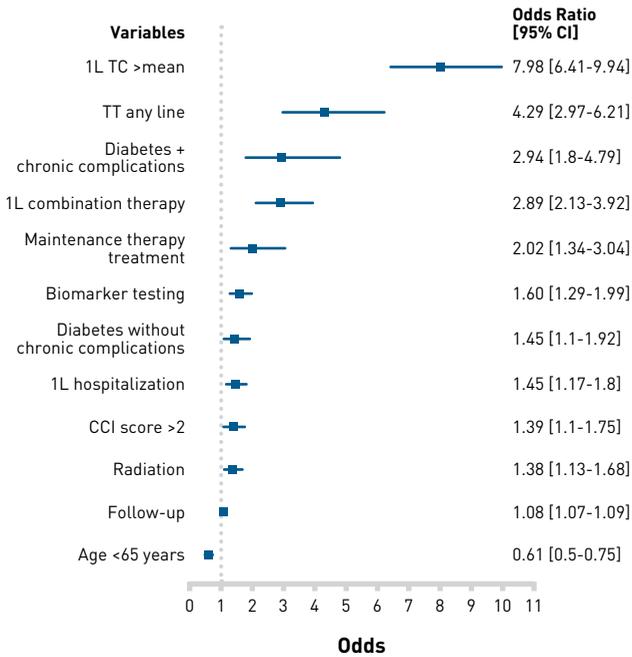
With few published studies evaluating TC among patients treated with novel therapies, drawing parallels to other research is difficult, particularly given the significant differences in time periods of analysis and patient populations. In 1 of the earliest

studies in this arena, Massachusetts General Hospital analyzed data from 1959 to 2010 and reported median direct medical cost per patient with any-stage NSCLC of \$40,500, with 63% of the costs occurring during the first year following diagnosis.²² The greatest expense category was chemotherapy (31%), followed by surgery (24%), inpatient medical services (17%), radiation therapy (12%), and diagnostics (5%).²² In the study, chemotherapy and acute care interventions were also the leading cancer-related expenses.²² Our estimate of TC was higher comparatively, which is likely explained by both period effects and inclusion of patients with disease at less-advanced stages in the older study.

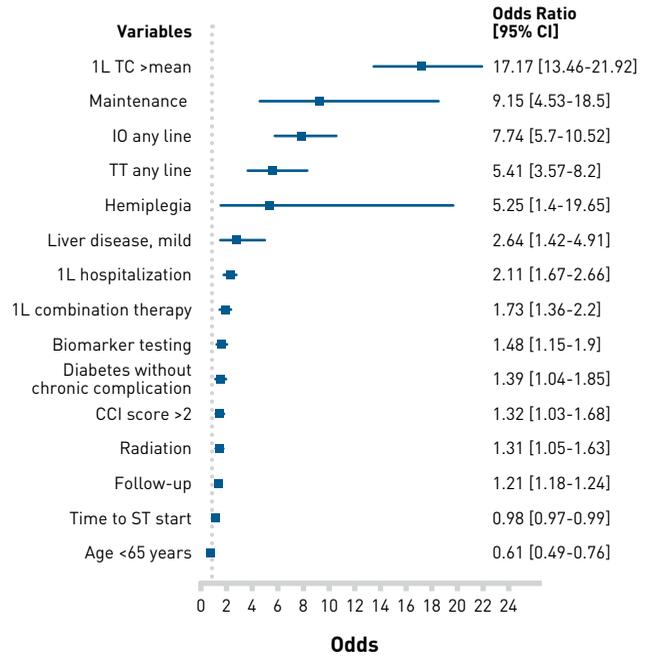
Two studies that included more recent patient populations evaluated the direct medical cost of NSCLC using the Surveillance Epidemiology and End Results Medicare database.³⁰⁻³¹ The first study, by Davis et al, included patients aged ≥65 years with metastatic squamous NSCLC diagnosed between 2001 and 2009, and it followed them through 2010.³⁰ This research found the mean total health care costs to be \$64,819. The second study, by Karve et al, examined metastatic NSCLC in patients diagnosed between 2000 and 2005, with follow-up through 2008, and reported that the mean lifetime TC from initiation of treatment was \$67,176.³¹ We observed significantly higher mean TC per patient, likely reflecting the increased costs of care over time, especially for patients covered by private employer-sponsored payers. In our study, approximately one-fourth of participants were covered with employer-sponsored payers and were not included in this Medicare-based analysis.

FIGURE 3. Predictors of Higher Total Cost

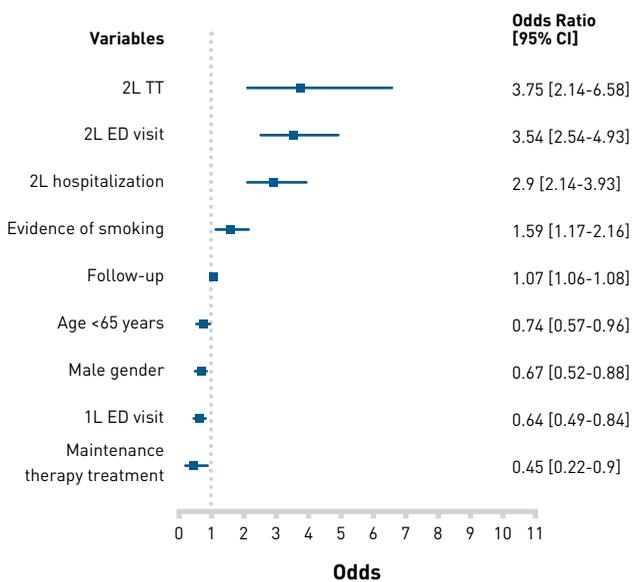
3a. Predictors of TC Above Mean Pre-IO



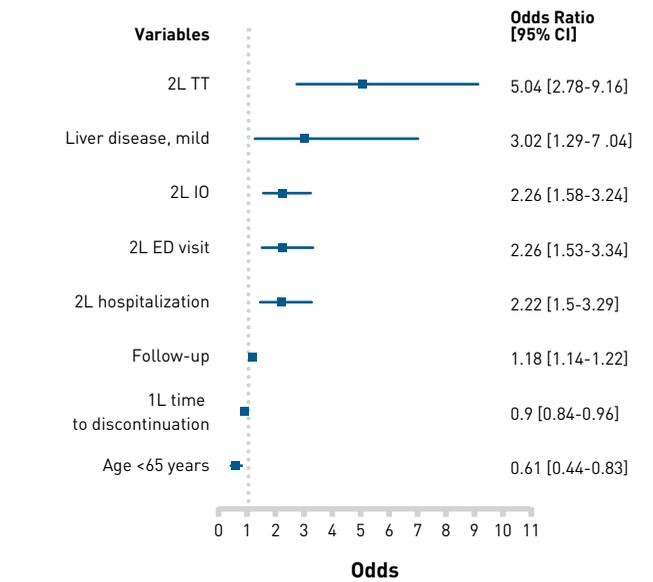
3b. Predictors of TC Above Mean Post-IO



3c. Predictors of 2L TC Above Mean Pre-IO



3d. Predictors of 2L TC Above Mean Post-IO



1L indicates first-line; 2L, second-line; CCI indicates Charlson Comorbidity Index; ED, emergency department; IO, immuno-oncology; TC, total costs; TT, targeted therapy.

Only 1 other study using multipayer claims data from 2000 to 2006 has been published. Vera-Llonch et al identified a mean TC over an average follow-up of 16.7 months (compared with 16.9 months for pre-IO patients in our analysis) of \$125,849 (95% CI, \$120,228-\$131,231), compared with \$165,548 pre-IO in our study.³² Twenty percent of costs were attributed to inpatient care (compared with 22% pre-IO in our study). Chemotherapy costs represented 22% of TC (compared with 16% among pre-IO in our study).³² Mean chemotherapy costs were \$27,924 compared with \$31,487 pre-IO in our study. Although costs appeared similar, particularly when adjusted for inflation, the Vera-Llonch et al study reported a lower number of hospitalizations (1.5 vs 2.5 pre-IO in our study) and a lower number of ED visits (1.6 vs 3.7).³² Comparing these pre-IO results with our research lends support to our post-IO period estimates and suggests that the increased pre-IO ST costs were likely driven by the introduction of targeted therapies into treatment. The same pattern was then seen with the introduction of IO; however, our results suggest that the higher cost of ST was offset by lower rates of inpatient admissions and lower costs overall.

The clinical benefit of IO in aNSCLC has been so profound that it was proclaimed the new standard of care at the American Society of Clinical Oncology 2018 Meeting.³³ This sea change in aNSCLC treatment also introduces a very relevant question in an era focused on value-based care: Can society afford this new treatment paradigm? In the past 3 years, 4 different IO drugs have received FDA approval in NSCLC with indications in adjuvant, first-line metastatic, and salvage settings, in both squamous and adenocarcinoma histologies. A combination of 2 IO agents, as well as IO plus chemotherapy trials, have demonstrated significant efficacy with manageable toxicity, likely heralding an IO backbone-based algorithm to NSCLC management in >90% of patients who lack a targetable mutation. The data presented in this study challenge concerns that innovative medicines will drive up TC in aNSCLC. Further research is warranted to evaluate the long-term clinical and financial impact of IO and other novel therapeutic entrants.

Limitations

Our study had several limitations typical of administrative claims-based, retrospective studies, such as selection bias and information bias. However, selection bias was likely limited, as our study included patients from both the Medicare- and Medicaid-eligible patient populations and those covered by employer-sponsored private insurance plans. Information bias, in this case the potential misclassification of disease and treatment, is a key concern owing to the lack of granularity to define histology or stage and the potential for misclassification of a line of therapy. To identify patients with aNSCLC in the absence of stage information in the study database, we relied on the presence of metastatic codes at diagnosis or initiation of ST within 6 months of diagnosis. Patients with a diagnosis of

SCLC may also have been inadvertently included to the extent that treatment regimens overlap; however, it is likely that this misclassification was nondifferential. It is possible that some early-stage patients receiving adjuvant therapy may have been included. Because data on treatment intent were not available, maintenance therapy was also assigned based on time to initiation following platinum-based or pemetrexed-based regimens, and it included therapies indicated for maintenance by the recent NCCN guidelines. The costs presented in this study were based on standardized allowed amounts and do not, necessarily, in the case of privately insured patients, represent the negotiated allowed payment between the insurer, provider, or institution for the services provided. This may result in downwardly biased estimates of the total costs of care. Finally, it is possible that the decline in hospitalization and ED visit rates are due to other factors beyond the introduction of IO therapy. Although certain factors, such as the evolution of the reimbursement from volume- to value-based care, may have played a role in our findings, new patterns of care beyond IO therapy have not emerged during the posttreatment period.

Conclusions

This study attempts to assess the TC among adult patients starting ST pre- and post approval of IO for aNSCLC to improve understanding as it pertains to the value of IO treatment. Our research explores this value debate by showing that, despite higher costs of ST, the lower rates of ED visits and hospitalizations, and thus their lower associated costs, favorably affect the total cost of care for patients with aNSCLC in the post-IO period. ■

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