

# Better Together? Costs of First-line Chemoimmunotherapy for Advanced Non–Small Cell Lung Cancer

Jonathan Kish, PhD, MPH; Djibril Liassou, MS; John Hartman, PhD; Solomon J. Lubinga, PhD; Dhruv Chopra, MS; and Bruce Feinberg, DO

**L**ung cancer is the second most common cancer and the leading cause of cancer death for men and women in the United States.<sup>1,2</sup> In 2018, deaths from lung cancer nearly outnumbered those from breast, prostate, colorectal, and brain cancers combined.<sup>3</sup> In 2021, more than 235,000 Americans received lung cancer diagnoses and 131,880 died from the disease.<sup>2</sup>

Although reductions in smoking, along with diagnostic and therapeutic advances, have resulted in a recent decline of lung cancer mortality rates of 5%, the 5-year survival rate among patients with newly diagnosed disease remains around 20%.<sup>2</sup> In 2015, the approval of the first immunotherapy (IO) drug, nivolumab, ushered in a new era of treatment for advanced non–small cell lung cancer (aNSCLC) with its indication as a second-line treatment.<sup>3</sup> This approval was shortly followed by the approval of pembrolizumab, which in October 2016 became the first IO agent approved in the first-line (1L) therapeutic setting for patients with a PD-L1 expression level of 50% or more.<sup>4</sup> Less than a year later in May 2017, the chemoimmunotherapy (IO+CT) regimen of pembrolizumab plus chemotherapy (CT) was approved for the 1L setting regardless of PD-L1 expression level.<sup>5</sup> Today, the landscape continues to evolve, including novel approved IO agents and combination IO therapies with and without a CT component.<sup>6,7</sup> In May 2020, nivolumab plus ipilimumab became the first combination IO+IO treatment approved for aNSCLC.<sup>8</sup>

The US health care system has historically imposed no restrictions on the reimbursement of cancer therapies based on cost-effectiveness. However, growing attention is being paid to treatment costs as a result of value-based care (VBC) initiatives such as the Oncology Care Model (OCM) and its replacement initiative, the Enhanced Oncology Model (EOM), which impose shared financial risk between providers and payers.<sup>9</sup> Moreover, the rapid expansion of high-cost, novel agents such as IO into the 1L setting for aNSCLC raises concerns about affordability, especially given the trend toward combination therapy. Drug price is typically the most important factor in sensitivity analyses of cost-effectiveness, yet other aspects of care such as office visits, infused drug administration, supportive care agents, and emergency and hospital care for

## ABSTRACT

**OBJECTIVES:** Recent advances have created options for first-line (1L) treatment of advanced/metastatic non–small cell lung cancer (aNSCLC). The study objectives were to describe the utilization of 3 classes of 1L treatment—chemotherapy (CT), immunotherapy (IO), and chemoimmunotherapy (IO+CT)—and the total, third-party payer, direct health care costs.

**STUDY DESIGN:** Retrospective, administrative claims database analysis of patients with aNSCLC who initiated 1L treatment between January 1, 2017, and May 31, 2019, with IO, CT, or IO+CT.

**METHODS:** Microcosting enumerated health care resource utilization, including antineoplastic drug costs, using standardized costs. Generalized linear models estimated per-patient per-month (PPPM) costs during 1L treatment, and adjusted cost differences in 1L among treatment cohorts were calculated using recycled predictions.

**RESULTS:** A total of 1317 IO-, 5315 CT-, and 1522 IO+CT-treated patients were identified. Utilization of CT declined from 72.3% to 47.6% between 2017 and 2019, replaced by use of IO+CT, which increased from 1.8% to 29.8%. Total PPPM costs in 1L were highest with IO+CT at \$32,436, compared with \$19,000 and \$17,763 in the CT and IO cohorts, respectively. Adjusted analyses showed that PPPM costs were \$13,933 (95% CI, \$11,760–\$16,105) higher in the IO+CT vs IO cohort ( $P < .001$ ) and IO costs were \$1024 (95% CI, \$67–\$1980) lower than CT ( $P = .04$ ).

**CONCLUSIONS:** IO+CT accounts for almost one-third of 1L aNSCLC treatment modalities, coinciding with a reduction in treatment with CT. Costs for patients treated with IO were lower than those for patients treated with both IO+CT and CT alone, driven primarily by antineoplastic drug and associated medical costs.

*Am J Manag Care.* 2023;29(5):e129–e135. doi:10.37765/ajmc.2023.89360

## TAKEAWAY POINTS

- ▶ Until recently, cytotoxic chemotherapy was the standard of care for patients with non–small cell lung cancer. Costs of cancer care, particularly for lung cancer, continue to rise with the introduction of novel therapies such as chemoimmunotherapy, the use of which has increased substantially since 2017.
- ▶ This cost and health care resource utilization analysis study provides the first estimates of the real-world, third-party payer costs comparing chemotherapy, immunotherapy, and chemoimmunotherapy to inform comparative value-based decision-making in earlier therapeutic settings.
- ▶ Compared with first-line immunotherapy or chemotherapy alone, combination chemoimmunotherapy for advanced/metastatic non–small cell lung cancer has significantly higher antineoplastic drug and associated medical costs.

adverse events (AEs) may contribute substantially to the economic burden of particular therapies.

Few studies have examined the differences in health care resource utilization (HCRU) or the total costs to third-party payers since the introduction of combination pembrolizumab plus CT in 2017.<sup>10</sup> It was our intent to focus on the cost impact of treatment preference for the vast majority of patients, in whom a driver mutation is not identified and for whom clinical practice guidelines support the use of varied therapeutic approaches. As such, drugs targeting the major genetic pathways involved (eg, EGFR, ALK, ROS1) were excluded from this study. Additionally, combination IO+IO therapies were excluded because the FDA approval was outside the designated study period, making any observed use off-label or within the context of a clinical trial. Therefore, the objectives of this study were to describe the treatment patterns, HCRU, and costs associated with adoption of 1L IO and IO+CT regimens since January 2017. We compared the adjusted differences in total all-cause costs during 1L therapy for patients treated with IO+CT vs IO monotherapy vs CT alone.

## METHODS

## Data Source

Medical and pharmacy claims from the Ability Patient Complete (APC) database were used to identify US patients 18 years or older who received aNSCLC diagnoses and initiated 1L systemic therapy with IO monotherapy, CT alone, or IO+CT agents between January 1, 2017, and May 31, 2019. The APC database is nationally representative, including claims during the past 5 years on 160 million covered patients from more than 150 payers across all states representing commercial health plan (~50%), Medicaid (~40%), and Medicare Advantage/supplemental sources. Claims-based selection criteria are described in **Figure 1**. Patients were required to have had a lung cancer diagnosis, have received a diagnosis of advanced/metastatic disease, and have initiated 1L systemic therapy with any IO monotherapy, CT alone, IO+CT, or targeted regimen approved for treatment of aNSCLC on or after January 1, 2017. Although patients who received a targeted treatment (eg, VEGF inhibitor, monoclonal antibody) were initially

selected, only the frequency of use over time was reported for these agents, and this study did not specify HCRU or cost-of-care analyses for them. Patients were identified as having aNSCLC if any claim included a diagnosis code for a distant lymph node or distant metastatic site. The database included the patients' full claims history through May 30, 2019.

## Line of Therapy and Study Cohorts

Line of therapy (LOT) assignment was made by grouping agents that were administered within 30 days of each other. Use of a new or additional agent, discontinuation of an agent

for at least 120 days, or a gap in the administration of an agent for more than 120 days formed a new LOT. Maintenance therapy was defined as the continuation of an IO agent (eg, pembrolizumab) following combination IO+CT, provided that the last claim for CT occurred within 120 days of the next claim for the IO agent. As such, maintenance therapy was not considered a new LOT, but a continuation of 1L therapy. Following LOT assignment, patients were categorized into 4 mutually exclusive cohorts based on the 1L treatment regimen received: (1) IO monotherapy, (2) IO+CT, (3) CT only, and (4) all other regimens (including targeted therapy).

## HCRU and Costs

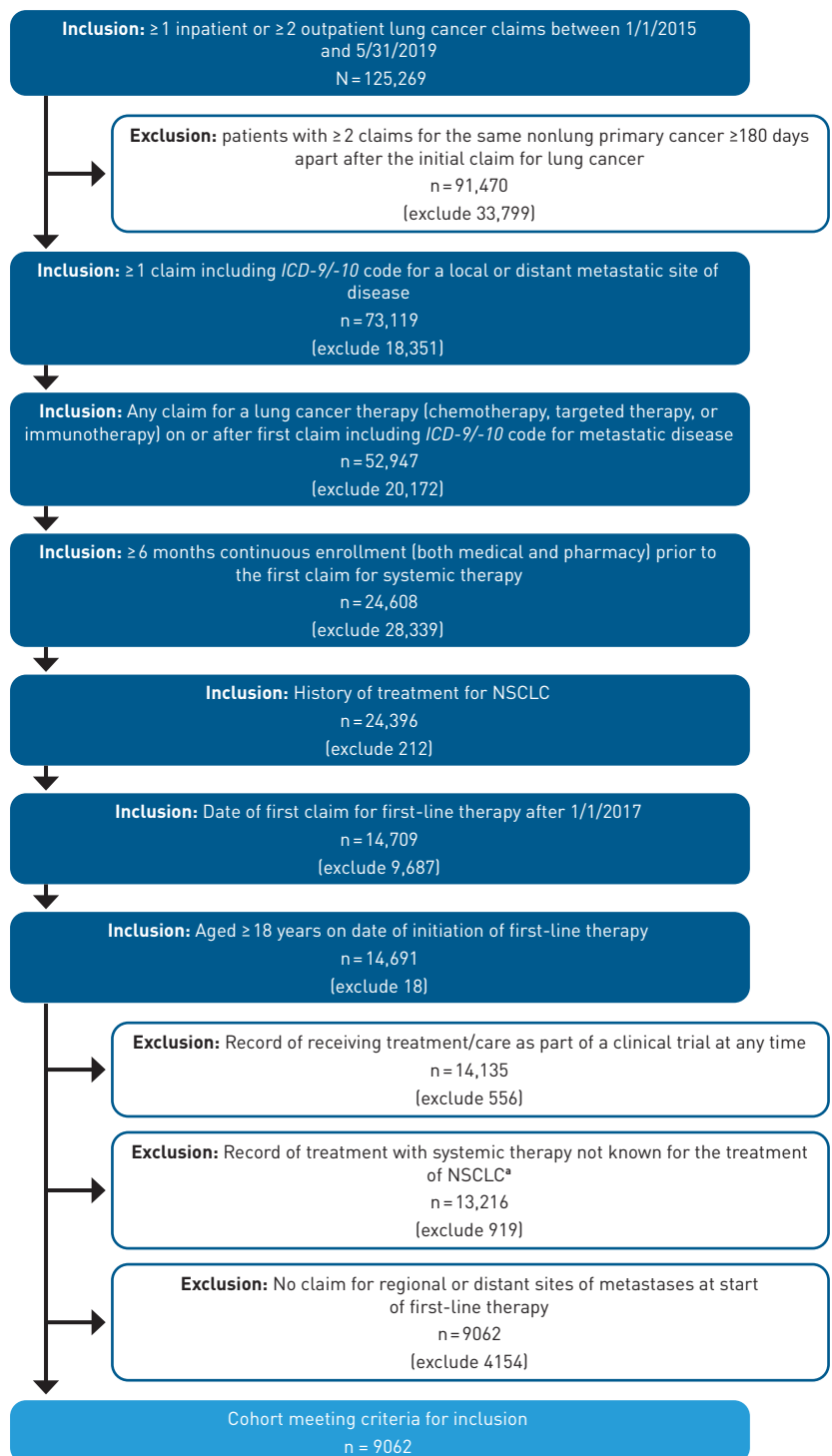
The study objectives were to estimate and compare the total costs of care during 1L therapy for patients by treatment cohort. Only patients treated with IO monotherapy, IO+CT, or CT alone were included in this portion of the analysis, as it was assumed that many patients treated with other regimens likely had *ALK* or *EGFR* mutations, and therefore their disease was not comparable with that of patients treated with IO or CT. For the 3 cohorts of interest, HCRU was first estimated per 1L therapy cohort based on the *Current Procedural Terminology* codes listed in the claims, which indicated the site of care where services were rendered. First, all hospital stays were identified, followed by emergency department (ED) visits, and the remainder of care was assigned to the outpatient/office setting. Next, a microcosting approach was taken to enumerate the per-patient costs of each medical or pharmaceutical service or product rendered in each setting during 1L therapy. Standardized unit costs from CMS fee schedules for medical services and average wholesale price (AWP) for pharmaceutical agents, including antineoplastics, were applied to each service.<sup>11-13</sup> Because units (ie, dose administered in mg/kg) were not uniformly available from the claims for IO therapies and other infused drugs, a standard dosage was applied to each antineoplastic drug claim (ie, mg/kg or mg/m<sup>2</sup> per schedule of administration using the average weight/height of US men/women). The cost was calculated as the standard dosage multiplied by the AWP. All costs were adjusted to an average of the Consumer Price Index for the United States in 2020.

## Statistical Analysis

Patient demographics and clinical characteristics were estimated in each cohort using descriptive statistical techniques including mean, SD, and median for continuous variables and counts and proportions for categorical variables. Statistical comparisons of demographics and clinical characteristics were not made among the cohorts, as it was not an objective of this research. Due to the potential variability in follow-up time (no minimum was required), exposure-adjusted estimates of HCRU and costs in the IL setting were calculated as per-patient per-month (PPPM). For HCRU and costs, the numbers of events (eg, inpatient admissions) or total dollars were divided by the total days of therapy and then multiplied by 30. Given that a cycle of systemic therapy (IO or CT) is 1 infusion every 2, 3, or 4 weeks, the total days of therapy value for patients with less than 1 month of follow-up was extrapolated to 30 in order to not artificially inflate PPPM estimates in cases where a patient had only 1 claim for systemic therapy.

Using the PPPM approach, 2 estimates of costs were calculated: (1) mean unadjusted PPPM, and (2) mean adjusted difference in costs among the 3 cohorts. First, the adjusted PPPM costs were estimated using a generalized linear model (GLM) with  $\gamma$  distribution and log-link function based on goodness-of-fit testing adjusted for sex, age at IL initiation, insurance payer type, US geographical region, time from first diagnosis to IL initiation, and Charlson Comorbidity Index (CCI) score. Next, the incremental adjusted mean differences in PPPM total health care costs and the respective individual component costs (eg, inpatient hospitalization, ED visit, office visit, and pharmacy) among the cohorts were calculated (ie, IO monotherapy vs IO+CT, IO monotherapy vs CT, and IO+CT vs CT) using the recycled predictions method.<sup>14</sup> Briefly, it isolates the effect of the treatment class on the outcome by holding constant the values for all other covariates, which in this case were sex, age at IL therapy initiation, payer, US region of residence, and CCI score. To obtain the mean values for the covariates, a probabilistic sampling technique was repeated 100 times in the patient population and a GLM was used to predict the PPPM costs. Next, the mean estimates were used as

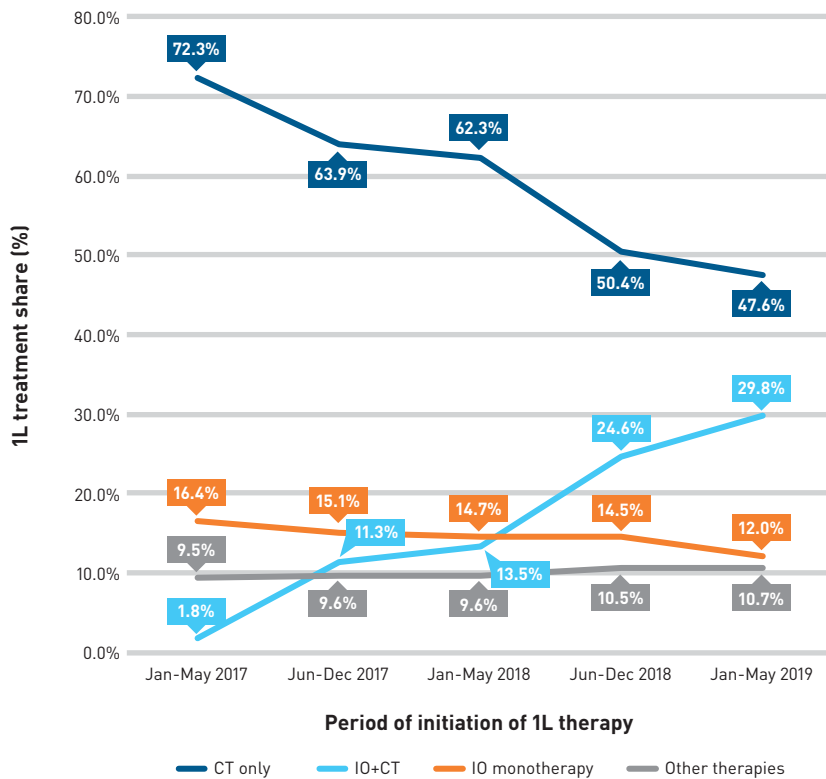
**FIGURE 1.** Patient Cohort Selection



ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, ICD, Tenth Revision; NSCLC, non-small cell lung cancer.

\*We identified 89 unique regimens among 919 patients that are not known as therapies for lung cancer. Examples include abiraterone, letrozole, panobinostat, and olaparib. Patients prescribed any of these therapies were likely to have a secondary cancer diagnosis that was not captured, and thus they were excluded.

**FIGURE 2.** CT, IO+CT, IO, and Other Therapy Utilization in the 1L Setting Over Time



1L, first-line; CT, chemotherapy; IO, immunotherapy; IO+CT, combination chemotherapy plus immunotherapy (ie, chemoimmunotherapy).

covariate parameters to calculate the incremental cost differences among the cohorts.

## RESULTS

Overall, 125,269 individuals were initially selected and 9062 (7.2%) met the study inclusion/exclusion criteria (Figure 1). The 1L therapy distribution of patients during the entire period was 14.5% receiving IO (n = 1317), 16.8% receiving IO+CT (n = 1522), 58.7% receiving CT (n = 5315), and 10.0% receiving other therapies (n = 908). The proportion of patients receiving CT declined from 72.3% in January through May 2017 to 47.6% during the corresponding months of 2019 (Figure 2). Use of IO+CT increased from 1.8% to 29.8% over the same interval, whereas use of IO therapies declined from 16.4% to 12.0% and use of other 1L therapies increased from 9.5% to 10.7%.

Patient characteristics were similar among those who received IO, IO+CT, and CT in 1L (Table 1). A slightly higher proportion of patients treated with IO+CT were male (54.7% vs 51.5% for IO and 50.9% for CT), whereas patients receiving IO were slightly older (median, 64 years) compared with those receiving IO+CT (62 years), and CT (63 years). Patients who received IO+CT had a lower CCI

score (mean of 1.8) compared with those who received IO or CT (mean of 2.1 for each).

The mean (SD) duration of 1L treatment (Table 1) was longest for IO-treated patients at 6.5 (7.3) months compared with IO+CT-treated patients at 5.6 (5.1) months and CT-treated patients at 3.0 (1.6) months. Treatment duration did vary according to the time of initiation (as follow-up time varied) but did so consistently across cohorts. Mean PPPM inpatient hospital admission and ED visit rates during 1L therapy were similar across the cohorts, at 0.23 and 0.34, respectively, for IO-treated patients, 0.24 and 0.37 for IO+CT-treated patients, and 0.23 and 0.35 for CT-treated patients. Mean PPPM outpatient physician office visits were 2.1 for the IO cohort, 2.5 for the IO+CT cohort, and 2.6 for the CT cohort (Table 1).

The mean unadjusted total health care PPPM costs during 1L therapy are shown in Figure 3 (including estimates for medical, pharmacy, and antineoplastic drug costs). The highest PPPM costs during 1L therapy were in the IO+CT cohort at \$32,436, compared with \$19,000 and \$17,763 in the CT and IO cohorts, respectively. Mean PPPM antineoplastic drug costs were highest in the IO+CT cohort at \$20,234, compared with \$2040 in the CT cohort and \$12,116 in the IO cohort. Associated medical costs (eg, office visits, hospitalizations, supportive care) were highest in the CT cohort

at \$13,178 and lowest in the IO cohort at \$2743.

Cost differences comparing each cohort are shown in Table 2. Adjusted analyses showed that PPPM costs were \$13,933 (95% CI, \$11,760-\$16,105) higher in the IO+CT cohort vs the IO cohort ( $P < .0001$ ). Further, PPPM medical costs were \$5876 higher and antineoplastic drug costs were \$7596 higher. Compared with CT costs, IO costs were \$1024 lower (95% CI, \$67-\$1980) ( $P = .04$ ), driven by substantially (\$10,265) lower medical costs notwithstanding substantially (\$10,025) higher antineoplastic drug costs for IO. As such, total health care PPPM costs in the IO+CT cohort were also higher by \$13,131 (95% CI, \$11,286-\$14,437) compared with those in the CT cohort.

## DISCUSSION

The last 5 years have seen expansive growth in the approved indications for IO in aNSCLC, which has led to meaningful improvements in clinical outcomes for patients. However, these improvements impose a cost on health care payers, patients, and society through government-subsidized health care plans. Research has demonstrated that at locally relevant willingness-to-pay thresholds, IO agents

are cost-effective.<sup>10</sup> Studies comparing IO+CT regimens with CT alone have reported similar findings and conclusions (albeit at varying levels of willingness-to-pay thresholds and quality-adjusted life-years),<sup>4,15,16</sup> but as far as we are aware, this research represents the first nationally representative real-world data study to estimate and compare the direct total health care costs to payers among IO, CT, and IO+CT regimens for 1L treatment of aNSCLC since the approval of IO in the 1L therapeutic setting.

We observed the direct impact of the introduction of IO therapy by first assessing its rate of adoption. Although the use of IO monotherapy in the 1L setting has remained relatively constant, the use of IO+CT has increased at a rate of more than 5% every 6 months between 2018 and 2019. Our data mirror the timing of the August 2018 approval of pembrolizumab plus CT for 1L treatment of aNSCLC, with a near doubling of the proportion of patients initiating 1L IO+CT between the first and second half of 2018 (99% of patients in the study sample had received pembrolizumab-containing regimens).<sup>4</sup> The observation that IO monotherapy use remained relatively constant may be explained by its preferred use in patients with high PD-L1 expression (although PD-L1 data were not available for analysis in this study), cost concerns for combination therapy (especially among providers participating in VBC initiatives such as OCM), and/or the inability of certain patients to tolerate CT. Consequently, IO monotherapy remains a relevant treatment approach for appropriate patients with aNSCLC (eg, those with  $\geq 50\%$  PD-L1 expression).

Next, we found that IO+CT-treated patients had the highest total PPPM health care costs in the 1L setting, which were significantly higher than those of patients treated with IO or CT. These findings were not explained by HCRU differences, as no statistically significant differences in hospitalizations or ED visits were found among the 3 cohorts. Instead, higher antineoplastic drug costs likely explain a large proportion of this difference, a phenomenon that has previously been reported with novel aNSCLC agents such as osimertinib, which was adopted into routine clinical practice and led to a 100% increase in total health care costs.<sup>17</sup> In addition, a possible explanation for the greater antineoplastic drug costs for the IO+CT cohort compared with IO monotherapy or CT alone may be driven by the use of pemetrexed, which remains unavailable in generic formulation in the United States. In the IO+CT cohort, more

than 80% of individuals received pembrolizumab in combination with pemetrexed, compared with less than 25% of patients in the CT cohort. In addition to the higher drug costs of pembrolizumab and pemetrexed, substantially (\$8860) higher PPPM medical costs for IO+CT were observed compared with the total PPPM medical costs for IO of \$2743. The difference may result at least in part from the association of CT with costs for the management of AEs, which may require supportive care interventions. The declining duration of 1L therapy over time in all cohorts may have been associated

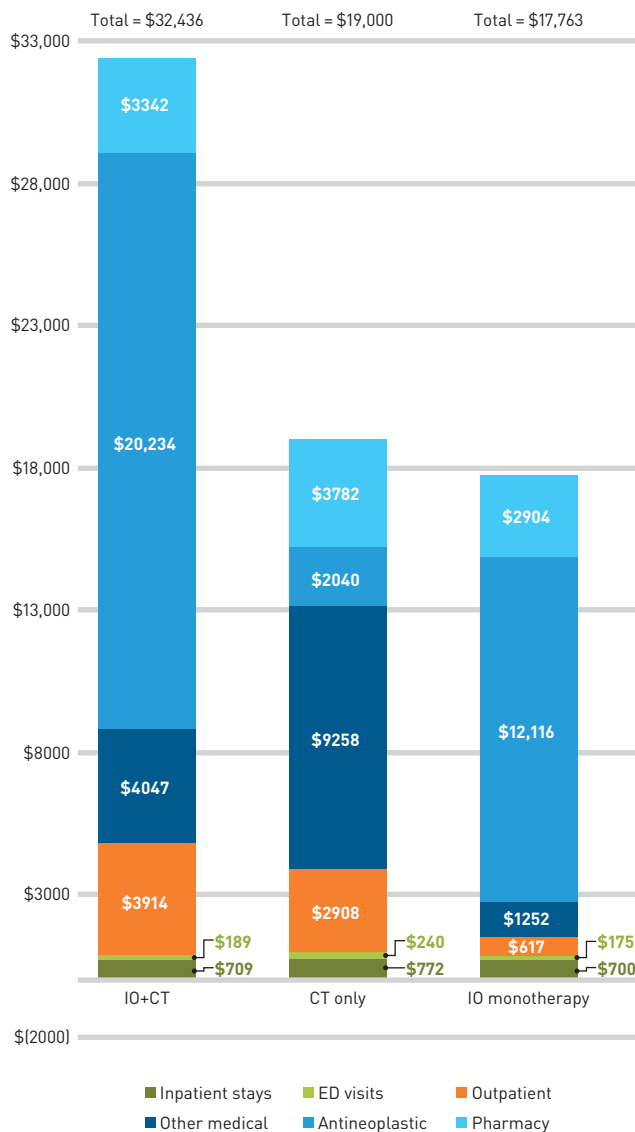
**TABLE 1.** Study Cohort Demographic, Clinical, and Treatment Characteristics

Characteristic	IO	IO+CT	CT only
	monotherapy n = 1317	combination n = 1522	n = 5315
Male, n (%)	678 (51.5%)	833 (54.7%)	2704 (50.9%)
Age in years at initiation of 1L therapy			
Mean (SD)	65.3 (9.9)	62.0 (8.9)	63.3 (9.3)
Median (range)	64 (21-89)	62 (28-88)	63 (20-88)
Payer, n (%)			
Commercial	415 (31.5%)	625 (41.1%)	1777 (33.4%)
Medicaid	423 (32.1%)	475 (31.2%)	1840 (34.6%)
Medicare Advantage/supplemental	404 (30.6%)	362 (23.8%)	1450 (27.3%)
Unknown	75 (5.7%)	60 (4.0%)	248 (4.7%)
US region of residence, n (%)			
Northeast	356 (27.0%)	368 (24.2%)	1209 (22.8%)
Midwest	317 (24.1%)	437 (28.7%)	1338 (25.2%)
South	236 (17.9%)	240 (15.8%)	1052 (19.8%)
West	407 (30.9%)	476 (31.3%)	1713 (32.2%)
Unknown	1 (0.1%)	1 (0.1%)	3 (0.1%)
Charlson Comorbidity Index score			
Mean (SD)	2.1 (1.8)	1.8 (1.6)	2.1 (1.8)
Median (range)	2.0 (0.0-12.0)	1.0 (0.0-10.0)	2.0 (0.0-12.0)
Follow-up in months from 1L initiation			
Mean (SD)	6.9 (7.1)	5.2 (4.8)	6.6 (5.9)
Median (range)	4.1 (1-28.8)	3.7 (1-28.5)	4.8 (1-28.8)
Duration of 1L therapy in months by date of initiation, mean (SD)			
Jan 2017-May 2017	6.5 (7.3)	4.7 (5.0)	3.0 (1.8)
Jun 2017-Dec 2017	6.5 (6.6)	5.6 (5.1)	2.9 (1.8)
Jan 2018-May 2018	5.1 (4.6)	3.6 (3.0)	3.0 (1.6)
Jun 2018-Dec 2018	3.9 (3.0)	4.3 (2.8)	2.9 (1.5)
Jan 2019-May 2019	1.8 (1.2)	2.1 (1.3)	1.9 (1.1)
PPPM HCRU during 1L therapy, mean (SD)			
Inpatient hospitalizations	0.23 (0.44)	0.24 (0.43)	0.23 (0.41)
ED visits	0.34 (0.56)	0.35 (0.53)	0.37 (0.58)
Office visits	1.96 (1.44)	2.37 (1.86)	2.43 (1.63)
Outpatient physician office visits	2.08 (1.39)	2.50 (1.82)	2.55 (1.57)

1L, first-line; CT, chemotherapy; ED, emergency department; HCRU, health care resource utilization; IO, immunotherapy; IO+CT, combination immunotherapy plus chemotherapy (ie, chemoimmunotherapy); PPPM, per-patient per-month.



**FIGURE 3.** Total PPPM Costs of 1L Therapy by Drug Class



1L, first-line; CT, chemotherapy; ED, emergency department; IO, immunotherapy; IO+CT, combination immunotherapy plus chemotherapy (ie, chemoimmunotherapy); PPPM, per-patient per-month.

with fewer patients in each category over time, shortened length of follow-up, or switches to different types of therapy if the current therapy was not efficacious as time continued.

Finally, we observed significantly higher medical costs for patients who received CT alone vs either IO or IO+CT. Further research is warranted to examine whether higher medical costs of CT alone may be related to inferior clinical outcomes for patients or whether these differences could be explained by systematic clinical differences among the cohorts. Patients in the end-of-life phase of cancer care,

**TABLE 2.** Mean PPPM Cost Differences (95% CIs) Among 1L Drug Regimens\*

Costs	Mean difference	Lower 95% CI	Upper 95% CI	P
<b>IO+CT vs IO monotherapy</b>				
All (medical + pharmacy)	\$13,933	\$11,760	\$16,105	<.0001
Medical	\$5876	\$4769	\$6983	<.0001
Inpatient stays	\$0	-\$128	\$128	.9961
ED visits	\$13	-\$16	\$42	.3772
Outpatient (physician office, clinic, outpatient hospital)	\$3138	\$2145	\$4131	<.0001
Other medical costs	\$2724	\$2266	\$3182	<.0001
Pharmacy	\$461	\$159	\$763	.0028
Antineoplastic drug costs	\$7596	\$5965	\$9227	<.0001
<b>IO monotherapy vs CT only</b>				
All (medical + pharmacy)	-\$1024	-\$1980	-\$67	.0360
Medical	-\$10,265	-\$11,124	-\$9406	<.0001
Inpatient stays	-\$77	-\$189	\$36	.1832
ED visits	-\$54	-\$113	\$5	.0745
Outpatient (physician office, clinic, outpatient hospital)	-\$2250	-\$2610	-\$1890	<.0001
Other medical costs	-\$7885	-\$8643	-\$7127	<.0001
Pharmacy	-\$783	-\$1080	-\$487	<.0001
Antineoplastic drug costs	\$10,025	\$9687	\$10,363	<.0001
<b>IO+CT vs CT only</b>				
All (medical + pharmacy)	\$13,131	\$11,826	\$14,437	<.0001
Medical	-\$4457	-\$5402	-\$3511	<.0001
Inpatient stays	-\$44	-\$151	\$63	.4185
ED visits	-\$38	-\$93	\$16	.1698
Outpatient (physician office, clinic, outpatient hospital)	\$928	\$347	\$1509	.0018
Other medical costs	-\$5302	-\$6029	-\$4575	<.0001
Pharmacy	-\$395	-\$670	-\$120	.0049
Antineoplastic drug costs	\$17,983	\$17,212	\$18,754	<.0001

1L, first-line; CT, chemotherapy; ED, emergency department; HCRU, health care resource utilization; IO, immunotherapy; IO+CT, combination immunotherapy plus chemotherapy (ie, chemoimmunotherapy); PPPM, per-patient per-month.

\*Probabilistic sampling approach was employed using PROC SURVEYSELECT in SAS version 9.4 (SAS Institute) to draw a 50% sample using simple random sampling (SRS without replacement). A PROC GLM model was run for the selected sample and the parameter estimates were recorded. The process was repeated for 100 random samples. The final model reports the mean of all parameter estimates obtained from 100 sample runs.

during which treatment with CT alone may be more frequent, incur direct medical costs substantially higher than those of patients in the continuing phase of treatment.<sup>18</sup>

**Limitations**

There are several limitations to the current study specifically and inherent to administrative claims-based analyses. First, HCRU and total PPPM cost estimates may be prone to error due to lack of complete follow-up. Second, paid costs were not available, and

drug reimbursement rates may vary by payer. Third, LOT assignment was based on an algorithm, and as such may be subject to misclassification. Strengths of this study include the large sample size and the representation of Medicaid patients in the APC database, which is higher than in other commercial claims-based databases.

## CONCLUSIONS

IO+CT in the 1L therapeutic setting now accounts for nearly a third of 1L aNSCLC treatment modalities, a shift that has coincided with a 25% reduction in the proportion of patients treated with 1L CT from 2017 to 2019. Additionally, the use of IO monotherapy has remained relatively constant at 12% to 16% during this interval. Patients treated with IO monotherapy had fewer outpatient visits PPPM, but no differences in hospital admissions or ED visits were observed among the 1L therapy cohorts. Further, CT-containing regimens were associated with higher nonantineoplastic health care costs than were IO monotherapy regimens. The transition to a VBC framework and shared financial risk payment models such as OCM warrants continued analyses of cost-effectiveness to provide patients, providers, payers, and policymakers the data needed to inform the design of benefit plans, shared decision-making, and optimized health care outcomes, both clinically and financially. Further research will help to stratify cost-effectiveness of the increasingly myriad therapeutic options for aNSCLC, which include CT, IO, and targeted therapies alone and in combination. ■

### Acknowledgments

The authors would like to acknowledge Alexandrina Balanean and Danielle Gentile of Cardinal Health for manuscript editing.

**Author Affiliations:** Cardinal Health (JK, DL, DC, BF), Dublin, OH; Bristol Myers Squibb (JH, SJL), Lawrenceville, NJ.

**Source of Funding:** This research was sponsored by Bristol Myers Squibb.

**Author Disclosures:** Dr Kish reports former employment and stock ownership in Cardinal Health. Mr Liassou reports employment at Cardinal Health. Dr Hartman reports employment and stock ownership in Bristol Myers Squibb, which is the manufacturer and patent owner of a competitor regimen. Dr Lubinga reports employment and stock ownership in Bristol Myers Squibb. Mr Chopra reports employment at Cardinal Health. Dr Feinberg reports employment and stock ownership in Cardinal Health.

**Authorship Information:** Concept and design (JK, JDH, SJL, DC, BF); acquisition of data (JK, DC); analysis and interpretation of data (JK, DL, JDH, SJL, DC, BF); drafting of the manuscript (JK, BF); critical revision of the manuscript for important intellectual content (JK, DL, JDH, SJL, BF); statistical analysis (JK, DL); obtaining funding (JDH); administrative, technical, or logistic support (SJL); and supervision (JK, JDH).

**Address Correspondence to:** Bruce Feinberg, DO, Cardinal Health, 7000 Cardinal Pl, Dublin, OH 43017. Email: bruce.feinberg@cardinalhealth.com.

## REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020;70(1):7-30. doi:10.3322/caac.21590
2. Cancer stat facts: lung and bronchus cancer. National Cancer Institute Surveillance, Epidemiology, and End Results Program. Accessed September 17, 2022. <https://seer.cancer.gov/statfacts/html/lungb.html>
3. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Engl J Med*. 2015;373(17):1627-1639. doi:10.1056/NEJMoa1507643
4. Pai-Scherf L, Blumenthal G, Li H, et al. FDA approval summary: pembrolizumab for treatment of metastatic non-small cell lung cancer: first-line therapy and beyond. *Oncologist*. 2017;22(11):1392-1399. doi:10.1634/theoncologist.2017-0078
5. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. *N Engl J Med*. 2018;379(21):2040-2051. doi:10.1056/NEJMoa1810865
6. Socinski MA, Jotte RM, Cappuzzo F, et al. Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. *N Engl J Med*. 2018;378(24):2288-2301. doi:10.1056/NEJMoa1716948
7. Wang C, Kulkarni P, Salgia R. Combined checkpoint inhibition and chemotherapy: new era of 1st-line treatment for non-small-cell lung cancer. *Mol Ther Oncolytics*. 2019;13:1-6. doi:10.1016/j.omto.2019.02.001
8. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Engl J Med*. 2019;381(21):2020-2031. doi:10.1056/NEJMoa1910231
9. Aviki EM, Schleicher SM, Mullangi S. The Oncology Care Model and other value-based payment models in cancer care. *JAMA Oncol*. 2019;5(3):298-299. doi:10.1001/jamaoncol.2018.5735
10. Dacosta Byfield S, Chastek B, Korrer S, Horstman T, Malin J, Newcomer L. Real-world outcomes and value of first-line therapy for metastatic non-small cell lung cancer. *Cancer Invest*. 2020;38(10):608-617. doi:10.1080/07357907.2020.1827415
11. Physician fee schedule: CY 2021 physician fee schedule update. CMS. Updated November 2, 2022. Accessed August 5, 2022. <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched>
12. Medicare Part B drug average sales price. CMS. Updated March 15, 2023. Accessed August 12, 2022. <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice>
13. Medi-Span Price Rx: online drug pricing tool. Wolters Kluwer. Accessed July 10, 2022. <https://www.wolterskluwer.com/cdi/ppc/pricerx/>
14. Li Z, Mahendra G. Using "recycled predictions" for computing marginal effects. Lex Jansen. Accessed October 26, 2022. <https://www.lexjansen.com/wuss/2009/hor/HOR-Li.pdf>
15. Courtney PT, Yip AT, Cherry DR, Salans MA, Kumar A, Murphy JD. Cost-effectiveness of nivolumab-ipilimumab combination therapy for the treatment of advanced non-small cell lung cancer. *JAMA Netw Open*. 2021;4(5):e218787. doi:10.1001/jamanetworkopen.2021.8787
16. Wan X, Zeng X, Peng L, et al. Cost-effectiveness analysis of nivolumab plus ipilimumab for advanced non-small-cell lung cancer. *Front Pharmacol*. 2021;12:580459. doi:10.3389/fphar.2021.580459
17. Whalen JJ, Eckwright DJ, Burke JP, Gleason PP. Osimertinib first-line approval in epidermal growth factor receptor (EGFR) mutation-positive metastatic non-small cell lung cancer (NSCLC): impact on utilization and total cost of care among 15 million commercially insured members. *J Manag Care Spec Pharm*. 2019;29(suppl 10-a):S30. doi:10.18653/jmcp.2019.25.10-a.s1
18. Kaye DR, Sung Min H, Herrel LA, Dupree JM, Ellimoottil C, Miller DC. Costs of cancer care across the disease continuum. *Oncologist*. 2018;23(7):798-805. doi:10.1634/theoncologist.2017-0481

Visit [ajmc.com/link/89360](http://ajmc.com/link/89360) to download PDF