Healthcare Cost and Resource Utilization among First-Line (1L) Treated Patients With Metastatic Non–Small-Cell Lung Cancer (mNSCLC): Analysis of SEER-Medicare Linked Claims in the US

RWD95

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Introduction

- The emergence of immune checkpoint inhibitors (ICIs) targeting the programmed cell death protein 1 (PD-1) pathway in the last decade has revolutionized the therapeutic paradigm for patients with metastatic NSCLC[1]
- Pembrolizumab, an anti–PD-1 therapy, has demonstrated significant improvements in overall survival compared to chemotherapy in pivotal clinical trials for patients with mNSCLC without EGFR mutations or ALK genomic tumor aberrations[2-4]
- Based on evidence from clinical trials (KEYNOTE-189, KEYNOTE-407) and real-world studies, pembrolizumab has become the preferred first-line (1L) treatments for patients with mNSCLC, either as monotherapy or in combination with carboplatin/cisplatin and pemetrexed for non-squamous (NSQ) mNSCLC or with carboplatin and taxane (paclitaxel/nab-paclitaxel) for squamous (SQ) mNSCLC.[1, 3-6] However, real-world data on healthcare resource utilization (HCRU) and costs among mNSCLC patients of varying histologies (eg, squamous, non-squamous) who are receiving 1L treatments is not well understood

Objective

To examine baseline characteristics, HCRU, and costs among mNSCLC patients overall and by histology (squamous and non-squamous) type and disease state (progression-free (PF) and progressed disease (PD)) following 1L treatment initiation

Methods

Study Design and Data Source

- A retrospective cohort study was conducted using claims data from Surveillance Epidemiology and End Results (SEER)-Medicare linked cancer database from 2007 to 2020 (ie, study period)

Study Population

- Eligible study population included mNSCLC [≥1 inpatient (IP)/emergency department (ED) visit claim, or ≥2 outpatient (OP) visit claims for lung cancer diagnosis ≥30 days apart] and metastatic staging (Stage IV per American Joint Committee on Cancer [AJCC 7th edition][7] patients aged ≥66 years with no prior history of systemic treatment who initiated 1L therapy between January 1, 2007 - December 31, 2019. Detailed patient selection criteria are outlined below:

Inclusion Criteria

- Patients should be continuously enrolled for ≥6 months in Medicare parts A, B, and D following mNSCLC diagnosis between 2007 - 2020, and
- Patients who initiated 1L therapy (chemotherapy, immuno-oncology (IO) monotherapy, or in combination, platinum/non-platinum)

Exclusion Criteria

- Patients without a diagnosis of stage IV NSCLC
- Patients with other cancer diagnosis (non-NSCLC) before the initial diagnosis of NSCLC
- Patients who have received previous systemic therapy
- Patients with <12 months baseline period (pre-index) and patients without continuous enrollment for 6 months in Medicare parts A, B, and D

Study Index, Pre-index and Post-index Time Period

- *Index date*: Defined as the date of 1L treatment initiation
- *Baseline period (Pre-index):* A minimum of 12 months preceding the index date (ie, patients who initiated 1L therapy)
- *Follow-up/observation period (Post-index):* A period between the index date and the earliest of the following:
  - (i) end of data availability ie, December 31, 2020, or
  - (ii) end of Medicare part A (inpatient), part B (outpatient), or part D (prescription drug coverage) eligibility, or
  - (iii) death

Study Cohorts Selection Criteria

- The eligible study population of 1L-treated mNSCLC patients were categorized into the following three study cohorts based on type of histology:
  - *Overall cohort:* Squamous and Non-squamous histology
  - *SQ cohort:* Squamous histology only
  - *NSQ cohort:* Non-squamous histology only

Study Measures and Definitions

The following measures were analyzed for the three study cohorts:

Baseline Measures (Pre-index)

- Demographics
- Clinical characteristics

Outcome Measures (Post-Index)

HCRU & Cost Outcomes

- All-cause, NSCLC-specific, possible adverse event (AE)-related, and other-cause related HCRU for different medical services [ie, IP, OP ED, and skilled nursing facility (SNF)] were examined as mean standardized HCRU rates and per-patient per-month (PPPM) rates
- All-cause, NSCLC-specific, possible AE-related and other-cause related costs for different medical services [ie, IP, OP, ED, and SNF] were determined from the total amount paid by Medicare, patients, and other payers, and reported as mean standardized PPPM costs

Statistical Methods

- Baseline demographics, clinical characteristics, and treatment outcomes were reported as frequencies and percentages for categorical variables and mean (SD), median (IQR), as well as 95% confidence intervals (CI) for continuous variables, as appropriate. The proportion of patients who initiated 1L therapy of interest, including pembrolizumab-containing regimens, was also reported
- Mean PPPM HCRU was calculated as the total visits divided by the total number of days of enrollment in the cohort, multiplied by 30 days
- Mean PPPM costs were calculated as the total costs divided by the total number of days of enrollment in the cohort, multiplied by 30 days
- Disease management (DM) costs were reported as mean PPPM costs for PF vs. PD and by year (Year 1, Year 2, Year 3, Years 4-5, Years 6+), whereas terminal care (TC) costs were calculated as mean PPPM costs
- All costs were inflation-adjusted to December 2023 US dollars based on the medical care component of the Consumer Price Index[8]

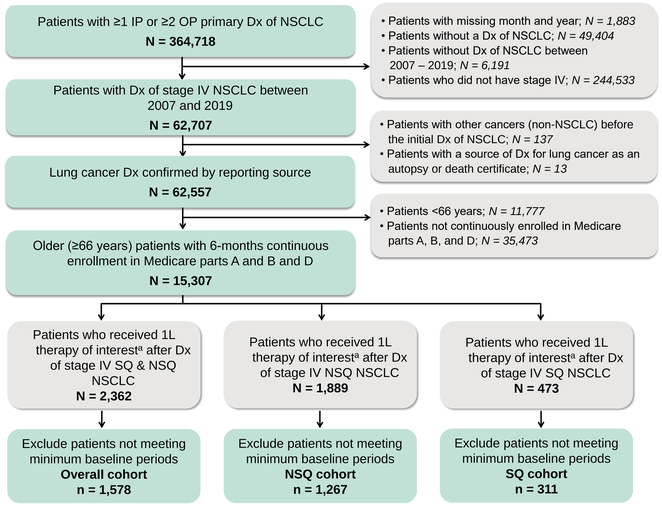
HCRU and Costs Definitions	
All-cause	HCRU or cost-related claims for the different medical services (eg, IP, ED, SNF, OP) for any reason and includes NSCLC-specific + possible AE-related + other-cause related claims
NSCLC-specific	HCRU or cost-related claims for different medical services (eg, IP, ED, SNF, OP) associated with an NSCLC diagnosis or NSCLC-specific anti-neoplastic treatments either in the primary-only (OP) or primary or secondary diagnostic position (IP, ED, and SNF)
Possible AE-related*	HCRU or cost-related claims for different medical services associated with diagnosis of possible Grade 3-4 AEs (which were reported in historical pembrolizumab clinical trials) that were identified either in the primary or secondary diagnostic position
Other-cause	HCRU or cost-related claims for different medical services excluding NSCLC-specific + possible AE-related claims. This includes visits related to other-medical conditions (eg, heart failure, pain, etc.)
Disease Management (DM) and Terminal Care (TC) Costs	
DM costs	Estimated as cost-related claims for different medical services as the sum of all-cause direct healthcare costs except for NSCLC-specific drug acquisition, drug administration and possible AE-related costs during the time spent in: (i) progression-free (PF) vs progressed disease (PD) state and (ii) disease state by year after the index date • PF state is defined as the time from 1L treatment initiation until either initiation of a second-line treatment, administrative censoring (end of follow-up), or 3 months prior to death • PD state is defined as time from index date to end of follow-up among patients receiving second-line treatment for lung cancer, excluding costs from the last 30 days of life
TC costs	Estimated as cost incurred within 30 days before death across different medical services (IP, ED, SNF, OP) and pharmacy services as sum of all-cause except NSCLC-specific drug acquisition and administration costs

*There could be a linkage to comorbidities

Results

- Patient selection and final sample for Overall, NSQ, and SQ cohorts are provided in **Figure 1**

Figure 1: Study Population Selection Criteria



1L, first-line; Dx, diagnosis; IO, immuno-oncology; IP, inpatient; NSCLC, non–small-cell lung cancer; NSQ, Non-squamous; SQ, squamous; OP, outpatient; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1

[a]Therapy of interest in 1L: Chemotherapy, IO mono/combo, platinum/non-platinum; PD1, PD-L1; minimum baseline periods: Patients with ≥12-month period preceding the index date

- Mean age was 75.5 years, with 49% male and 84.5% White in the overall cohort (n=1,578). SQ (n=311) and NSQ (n=1,267) cohorts had similar demographics, except SQ had a higher proportion of males (60.7%) (**Table 1**)
- Approximately 30% of patients in the overall, NSQ, and SQ cohorts received pembrolizumab monotherapy while nearly one-third received pembrolizumab in combination with other regimens. In total, two-thirds of patients in the overall, NSQ, and SQ cohorts had initiated 1L treatment with pembrolizumab containing regimens, respectively
- All-cause, NSCLC-specific, and other-cause HCRU and cost outcomes are described in **Table 2** and **Figure 2**, respectively
- The overall all-cause PPPM HCRU was highest for OP visits (2.03), followed by ED visits (0.26), IP admissions (0.18), and SNF visits (0.03). Among these, NSCLC-specific PPPM HCRU were (0.86, 0.04, 0.04, 0.01), possible AE-related (0.13, 0.08, 0.06, 0.01), and other-cause (1.04, 0.13, 0.08, 0.01), respectively. HCRU patterns were similar for SQ and NSQ cohorts

Results

Table 1. Baseline Demographic and Clinical Characteristics among Overall, NSQ and SQ Cohorts

Demographics	Overall cohort (N = 1,578)	NSQ cohort (N = 1,267)	SQ cohort (N = 311)
Age			
Mean (SD)	75.53 (6.30)	75.49 (6.63)	75.70 (6.09)
Sex, n (%)			
Female	774 (49.05)	585 (46.17)	189 (60.77)
Race, n (%)			
White	1,334 (84.54)	1,083 (85.48)	251 (80.71)
Asian	114 (7.22)	82 (6.47)	32 (10.29)
African American	116 (7.35)	90 (7.10)	26 (8.36)
Other	*	*	*
Geographic region, n (%)			
Northeast	339 (21.48)	277 (21.86)	62 (19.94)
Midwest	194 (12.29)	155 (12.23)	39 (12.54)
South	369 (23.38)	288 (22.73)	81 (26.05)
West	676 (42.84)	547 (43.17)	129 (41.48)
Time from NSCLC diagnosis to index date (months)			
Mean (SD)	1.33 (0.62)	1.33 (0.62)	1.34 (0.59)
Charlson comorbidity index			
Mean (SD)	5.97 (3.51)	6.05 (3.44)	5.65 (3.79)

NSCLC, Non-small cell lung cancer; NSQ, Non-squamous; SQ, Squamous; SD, Standard deviation
*Cell sizes below 11 are suppressed

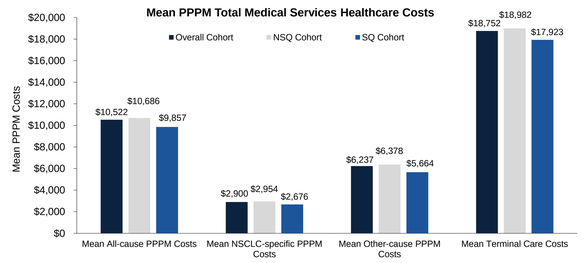
Table 2. Health Care Resource Utilization among Overall, NSQ and SQ Cohorts

Mean PPPM HCRU by service type	Overall cohort (N = 1,578)	NSQ cohort (N = 1,267)	SQ cohort (N = 311)
All cause PPPM (SD)			
Inpatient	0.18 (0.22)	0.18 (0.21)	0.20 (0.22)
Skilled nursing facility	0.03 (0.08)	0.03 (0.08)	0.03 (0.07)
Emergency department	0.26 (0.30)	0.25 (0.29)	0.28 (0.30)
Outpatient	2.03 (1.48)	2.01 (1.45)	2.13 (1.62)
NSCLC-specific PPPM (SD)			
Inpatient	0.04 (0.10)	0.04 (0.10)	0.04 (0.10)
Skilled nursing facility	0.01 (0.04)	0.01 (0.05)	0.01 (0.40)
Emergency department	0.04 (0.10)	0.04 (0.10)	0.04 (0.11)
Outpatient	0.86 (0.85)	0.85 (0.81)	0.91 (1.00)
Other-cause PPPM (SD)			
Inpatient	0.08 (0.13)	0.08 (0.13)	0.09 (0.14)
Skilled nursing facility	0.01 (0.05)	0.01 (0.05)	0.01 (0.04)
Emergency department	0.13 (0.18)	0.13 (0.18)	0.15 (0.18)
Outpatient	1.04 (0.93)	1.04 (0.93)	1.04 (0.93)

NSCLC, Non–small-cell lung cancer; NSQ, Non-squamous; SQ, squamous; PPPM, per-patient-per-month; SD, standard deviation; Note: HCRU is calculated as a percentage of the total population (patients ≥ 0 utilization/costs) between index date to observation end date

- PPPM medical costs were similar across the cohorts (all-cause $9,857-$10,686, NSCLC-specific $2,676-$2,954, possible AE-related $1,353-$1,517, other-cause $5,664-$6,378) as were mean TC costs ($17,923-$18,982)

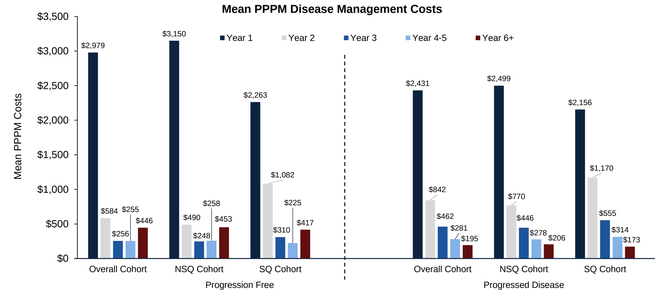
Figure 2. Total Medical Services Healthcare Costs among Overall, NSQ and SQ Cohorts



NSCLC, Non–small-cell lung cancer; NSQ, Non-squamous; SQ, squamous; PPPM, Per-patient-per-month
Note: Costs calculated as a percentage of the total population (patients ≥ 0 utilization/costs) between index date to observation end date. Total Medical Costs include costs across IP+ED+OP+SNF. Terminal care costs exceptions: patients who die within 3 months of the index date were directly included in terminal care cost calculations

- Specifically, costs for all-cause ($5,826-$6,619), NSCLC-specific ($1,946-$2,098) and other-cause ($3,723-$4,592) were higher in outpatient visits when compared to other medical services across the cohorts
- In year 1, DM PPPM costs varied from $2,156 to $2,499 for progressed patients and from $2,263 to $3,150 for progression free, with PPPM costs largely decreasing over time (**Figure 3**)

Figure 3. Annual Disease Management Costs among Progression Free vs Progressed Patients



NSQ, Non-squamous; SQ, squamous; PPPM, Per-patient-per-month
Note: Disease management costs exceptions: patients who die within 3 months of the index date were directly included in terminal care cost calculations. Disease management costs include costs across different medical services (IP+ED+OP+SNF)

Limitations

- As with any analysis using claims data, this study has limitations related to under coding or miscoding. Additionally, the data may not capture the most up-to-date treatment patterns and costs given that most recent data is available only up to 2020
- The database may not be generalizable to a younger population below 65 years of age
- Information regarding patient performance status such as The Eastern Cooperative Oncology Group (ECOG) and Programmed Death-Ligand 1 (PD-L1) expression levels is also not captured, thus limiting the depth of analysis and ability to draw inferences
- Furthermore, it is not possible to assess the association between therapy and AEs. Given the nature of claims data intended for billing and reimbursement purposes as well as the costs presented as bundled payments, there could be misclassification resulting in the possible AE-related costs reported in this study as being overestimated
- This is both due to inclusion of secondary diagnoses codes and the co-occurrence of possible AE-related costs along with underlying comorbidities costs which suggests that actual AE-related costs could be much lower than reported and is an area that warrants further investigation
- Finally, it should be noted that costs were not inflation adjusted to reflect 2025 USD and may consequently report lower values than actual estimates

Conclusions

- In this analysis of mNSCLC patients with overall, NSQ, and SQ histology, the majority of patients initiated 1L treatment with pembrolizumab-containing regimens
- Across the three cohorts, all-cause, NSCLC-specific, and other-cause costs were mainly driven by outpatient visits, while possible AE-related costs were driven by inpatient admissions
- Regardless of progression status, relative to later years, year 1 DM costs were highest for all patients, reflecting greater disease management intensity

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Disclosures

Authors Babel, Wehler, and Chirovsky report employment with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and stock ownership of Merck & Co., Inc., Rahway, NJ, USA.

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