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Real-world treatment patterns and costs in a US Medicare population with metastatic squamous non-small cell lung cancer

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ABSTRACT

Objectives: Despite advances in the treatment of nonsquamous non-small cell lung cancer (NSCLC), therapeutic choices and overall disease course for squamous NSCLC have remained relatively unchanged over the past several years. We provide a detailed account of current treatment patterns, healthcare use, and survival in real-world clinical settings for metastatic squamous NSCLC.

Materials and methods: Patients aged ≥65 years with metastatic squamous NSCLC diagnosed 2001–2009 were identified and followed through 2010 using the Surveillance, Epidemiology and End Results-Medicare database. Treatment patterns were descriptively analyzed. Multivariate logistic regressions were estimated to identify predictors of treatment pattern events; generalized linear models were estimated for total all-cause and NSCLC-related costs to assess cost drivers.

Results: Of 17,133 patients, 72% received cancer-directed therapy (surgery, radiation, chemotherapy, or biologic therapy), whereas 28% received only supportive care. Median survival was significantly longer in patients receiving cancer-directed therapy (8 months) than in patients receiving supportive care only (2 months) ($P < 0.0001$). An agent-specific first-line chemotherapy regimen was identified for 91% of the 7700 patients who received chemotherapy. Among these, the most common first-line regimen was carboplatin-paclitaxel combination therapy (46%). Common second-line regimens were gemcitabine monotherapy (16%) and pemetrexed monotherapy (11%). Factors associated with decreased odds of receiving cancer-directed treatment were black versus white race (OR, 0.72; 95% CI, 0.64–0.82), residence in the West versus South (OR, 0.73; 95% CI, 0.66–0.81), and metastatic disease at initial diagnosis versus progression to metastatic disease (OR, 0.77; 95% CI, 0.70–0.84).

Conclusions: Our study shows that prognosis remains poor for patients with metastatic squamous NSCLC, even among those receiving treatment, but particularly for patients limited to supportive care only, highlighting the continuing unmet medical need in this population. Additionally, our analysis indicates that selections for second-line and third-line chemotherapies are not necessarily consistent with National Comprehensive Cancer Network guidelines.

1. Introduction[1]

Lung cancer is the most common lethal cancer in the United States (US), with an estimated 220,000 new cases diagnosed in 2011 and 156,000 deaths [1]. Nearly two-thirds of all lung cancer cases are diagnosed at age 65 years or older [2]. Approximately 87% of lung cancer diagnoses are classified as non-small cell lung cancer

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[1] BAC, bronchioloalveolar; CCI, Charlson Comorbidity Index; ICD-9-CM, International Classification of Diseases, Ninth Edition, Clinical Modification; ICD-O-3, International Classification of Diseases for Oncology, Third Edition; NCCN, National Comprehensive Cancer Network; SEER, Surveillance, Epidemiology, and End Results.

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(NSCLC) [3], of which about 30% are of squamous histologic subtype [4]. Approximately 4 in 5 patients with a diagnosis of NSCLC in the US will have metastases either at the time of presentation or later in the course of their disease [5].

For metastatic NSCLC patients treated with standard platinum-based chemotherapy, median survival is 8–10 months [6]. Prognosis is worse for squamous histologic subtype than for non-squamous subtypes. A study of Surveillance, Epidemiology, and End Results (SEER)–Medicare data from 1998 to 2003 reported that 1-year survival among stage IV NSCLC patients was only 14.6% for squamous subtype compared to 18% for nonbronchioloalveolar (non-BAC) adenocarcinoma and 29.1% for BAC adenocarcinoma subtypes [7]. Two other studies in advanced-stage NSCLC compared survival between different treatment arms within each histology subtype [8,9], although no direct comparison of survival was made by histology subtype. Overall survival and treatment response were generally lower for squamous than for nonsquamous subtypes [8,9].

Despite significant advances in the treatment of metastatic NSCLC [10–15], newer treatments are effective mostly for patients with nonsquamous NSCLC [4]. Poor survival, lack of therapeutic advances for squamous NSCLC, and continued growth of the elderly US population necessitate assessment of current treatment patterns and quality of care in the real-world population.

Observational studies have examined treatment patterns, healthcare utilization, and direct medical costs associated with lung cancer, but most focused on all types of lung cancers combined [16–20] and were limited to chemotherapy costs with little information on survival, resource utilization, and costs for other services [21–24]. Data are particularly limited on resource use, cost, and survival differences between alternative regimens used in different therapy lines for squamous NSCLC in real-world settings.

Hence our objectives were to assess (1) demographic and clinical characteristics, (2) overall survival by treatment status, (3) treatment patterns and common systemic treatment regimens used in different therapy lines, and (4) healthcare resource use and costs among metastatic squamous NSCLC patients enrolled in the US Medicare system. Our findings may help inform future cost and cost-effectiveness assessments of newer, targeted therapies for squamous NSCLC.

2. Materials and methods

2.1. Data source

Retrospective data were taken from the SEER-Medicare linked database in the US, which combines clinical information from the SEER cancer registry with longitudinal medical and pharmacy claims data for Medicare Part A and Part B enrollees. SEER-Medicare data have been widely adopted for studies of this type and have been extensively described elsewhere [25–28]. The study was reviewed and approved by the RTI Institutional Review Board.

2.2. Patient selection

Patients with metastatic squamous NSCLC diagnosed initially at stage IV throughout the study period (January 1, 2001–December 2009) or at stage IIIB with pleural effusion during 2004–2009 (information on presence of pleural effusion was not present in registry data for 2001–2004) were selected for inclusion based on published classification criteria [29,30]. Additionally, patients whose initial diagnosis was at other stages of disease who later developed metastases (as evidenced by ICD-9-CM codes for secondary malignancy: 196.xx, 197.0, and 198.xx) were included. These patients were followed from the time of their metastatic diagnosis. Designation of cases as non-small cell or squamous histology was based on ICD-O-3 codes used in published literature [31–35].

An overall study index date was defined as the date of the first observed diagnosis of metastatic squamous NSCLC. Except for baseline patient characteristics, all study measures were followed on each patient from the index date until the earliest of death or study completion (end of the Medicare claims database: December 31, 2010). Based on the index date, patients were required to meet the several additional inclusion criteria as shown in Fig. 1.

2.3. Study measures

2.3.1. Patient characteristics

Demographics measured at the index date included age, sex, race, and US Census region. Disposition of patients' metastatic diagnosis (i.e., initially diagnosed with metastatic disease versus progressed to metastasis), disease stage, and tumor size at index as well as vital status at study completion also were reported. We also computed the Charlson Comorbidity Index (CCI) over the 6-month pre-index period, to obtain a measure of patients' overall baseline comorbidity status [38]; cancer diagnoses (any type) were excluded from the CCI algorithm. Finally, patients' treatment status was defined as receipt of at least one type of cancer-directed treatment (surgery, radiation, chemotherapy, or biologic therapy) during follow-up versus receipt of supportive care only (i.e., no cancer-directed treatments received during follow-up).

2.3.2. Treatment patterns

For patients who received any form of cancer-directed therapy, the prevalence of each treatment type received at any time during study follow-up was estimated and reported. These treatments were defined using relevant procedure and diagnostic codes (see Appendix A) captured in the linked Medicare claims data. We additionally assessed specific first-, second-, and third-line systemic (chemotherapy and/or biologic therapy) treatment patterns, as well as the distribution of regimen compositions observed in each therapy line. Systemic therapy regimens and cycles were defined using previously published methods [19,39,40].

2.3.3. Healthcare utilization and costs

Among patients who received cancer-directed therapy, total and average monthly all-cause and NSCLC-related healthcare utilization and costs were estimated and reported by care setting/service type. Additionally, for patients initiating an identifiable systemic therapy regimen, costs were reported by phase of care. Costs were adjusted at the claim-level to 2012 US dollars using the medical component of the US Consumer Price Index.

For the five most commonly observed first-line systemic treatment regimens, we additionally calculated and reported the number of treatment cycles administered and duration of treatment from initiation of the first cycle until completion of the last-observed cycle. Based on the total costs and cycles observed, average cost per cycle (including drug costs, provider fees, and facility costs as incurred during therapy administrations) was also estimated. Finally, total and disease-related costs incurred during predefined periods of patient follow-up were also assessed.

2.4. Statistical analyses

Descriptive univariate analysis was performed for all study measures. Statistical differences in patient characteristics by treatment status were assessed using Student's *t*-tests for continuous measures and chi-square tests for categorical measures. The Kaplan–Meier method (unadjusted for covariates) was used to